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PREFACE

GASTROENTEROLOGY ABSTRACTS and CITATIONS is a publication of the National Institute of Arthritis, Metabolism and Digestive Diseases. This specialized information medium has been initiated to fill an existing great need in the field of gastroenterology and to assist the Institute in meeting its obligations to foster and support laboratory and clinical research into the nature, causes, and therapy of diseases of the gastrointestinal tract. Publication GASTROENTEROLOGY ABSTRACTS and CITATIONS makes available citations of all current papers relevant to this field from medical journals published throughout the world. Approximately one-third of the citations dealing with the major aspects of gastroenterology have accompanying abstracts.

The issuing of GASTROENTEROLOGY ABSTRACTS and CITATIONS under the auspices of the National Institute of Arthritis, Metabolism, and Digestive Diseases will provide a much needed current awareness tool to scientists and will facilitate greater integration of research and clinical efforts in this field. The number and great diversity of publications in the area of gastroenterology makes it imperative that an appropriate service be available to investigators and practitioners so that they may be apprised of progress with a minimum of delay. Our aim is to provide the readers with a readily systematized complilation of current published work. The publication will provide the greatest usefulness if these interested investigators will contribute their ideas and comments for consideration whenever possible.

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The Secretary of the Department of Health, Education, and Welfare has determined that the publication of this periodical is necessary in the transaction of the public business required by law of this Department. Use of funds for printing this periodical has been approved by the Director of the Office of Management and Budget through April 30, 1975.

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NOTE

Journal names are abbreviated according to the list of abbreviations used by *Index Medicus*. For journals not covered by *Index Medicus*, the abbreviations (with some modifications) found in *World Medical Periodicals*, 3rd Edition, are used.

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans
Ar.	Arabic
Bul.	Bulgarian
Ch.	Chinese
Cz.	Czech
Dan.	Danish
Dut.	Dutch
E.	English
Eston.	Estonian
Fin.	Finnish
Fl.	Flemish
Fr.	French
Ger.	German
Gr.	Greek
Heb.	Hebrew
Hun.	Hungarian
Ic.	Icelandic
In.	Indonesian
It.	Italian
Jap.	Japanese
Kor.	Korean
Latv.	Latvian
Lith.	Lithuanian
Nor.	Norwegian
Pol.	Polish
Por.	Portuguese
Rum.	Rumanian
Rus.	Russian
Ser.	Serbo-Croatian
Sl.	Slovak
Sp.	Spanish
Sw.	Swedish
Th.	Thai
Turk.	Turkish
Uk.	Ukrainian
Viet.	Vietnamese

ABBREVIATIONS USED IN ABSTRACTS

ACTH	adrenocorticotropic hormone
ADP	adenosine diphosphate
AMP	adenosine monophosphate
ATP	adenosine triphosphate
BSP	sulfobromophthalein
C	degrees centigrade
cm	centimeter(s)
CNS	central nervous system
cpm	counts per minute
DNA	deoxyribonucleic acid
e.g.	for example
g	gram(s)
μg	microgram(s)
hr	hour(s)
i.m.	intramuscular
i.p.	intraperitoneal
IU	international unit(s)
i.v.	intravenous
kg	kilogram(s)
LD$_{50}$	median lethal dose(s)
LDH	lactic acid dehydrogenase
m	meter(s)
M	molar
mEq	milliequivalent(s)
mM	millimolar
μM	micromolar
mC,μC	milli- ,microcurie(s)
mg	milligram(s)
min	minute(s)
ml	milliliter(s)
mm	millimeter(s)
MTD	maximum tolerated dose
ng	nanogram (10^{-9})
pg	picogram (10^{-12})
p.o.	orally
ppm	parts per million
r	Roentgen
RBC	red blood cells (erythrocytes), red blood count
resp.	respectively
Rev.	review (only in citations)
RNA	ribonucleic acid
s.c.	subcutaneous
sec	second(s)
SGOT	serum glutamic-oxalacetic transaminase
SGPT	serum glutamic-pyruvic transaminase
U	unit(s)
UV	ultraviolet
WBC	white blood cells (leukocytes), white blood count
yr	year(s)

PRE-CLINICAL SCIENCES

MORPHOLOGY, CELLULAR STRUCTURE AND HISTOCHEMISTRY

5528 ISOLATION OF A HUMAN GASTROINTESTINAL MEMBRANE ANTIGEN. *(Fr.)* Clausell, D. T.; Burtin, P. (Inst. Biol. Res., Rio Grande do Sul Univ., Porto Alegre, Brazil). *Ann. Immunol. (Paris).* 124C(1):17-26, 1973.

Homogenates, prepared from the mucosa of 22 normal stomachs and from 32 gastric epitheliomas, were centrifuged at 20,000 g for 20 min and the centrifuged deposit was solubilized with a solution of Triton X100 by the method of Kandutsch. After purification by filtration on Sephadex G-75, an antigen was isolated which was identified as a glycoprotein and which, on electrophoresis, was shown to have a molecular weight of about 45,000. When injected into rabbits, solubilized antigen from normal gastric mucosa produced antibody titers of 1:6. Immunofluorescence studies demonstrated that this antigen is present in the cytoplasm and cell membranes of mucosa from the small intestine and colon and fetal stomach and small intestine, but not in the esophageal or gallbladder mucosa or in malignant gastric or colonic tumors. Solubilized extracts from gastric epitheliomas contained carcinoembryonic antigen which was not detected in the cell membranes of normal gastric mucosa by immunofluorescence.

5529 CHANGES IN DESQUAMATION RATE OF JEJUNAL EPITHELIUM IN CATS DURING FASTING. *(E.)* Goldsmith, D. P. J. (Coll. Med., Univ. Nebraska, Omaha). *Digestion* 8(2):130-141, 1973.

The desquamation rate of jejunal epithelial tissue was studied in fasting cats by measuring the rate of accumulation of DNA in the luminal fluid. The applicability of the method was first determined by calculating a turnover time for the tissue from the rate of accumulation of DNA and comparing it with turnover time calculated by the colchicine method. The 2 values agreed. When female cats were fasted, the desquamation rate decreased markedly and progressively over 256 hr when it had decreased to about 18% of normal. There was no accompanying change in epithelial cell mass or protein content. The desquamation rates after 64-256 hr of fasting were statistically lower than after 16-40 hr of fasting. In animals who were refed after 184 hr fasts, the desquamation rates were spread over a relative wide range of values, indicating the epithelium was returning to normal. It is suggested that this apparent ability of the epithelium to remain in a dormant state without loss of cells during fasting allows it to begin its normal physiological processes when food again becomes available. Thus, only small amounts of very valuable amino acids are used for rebuilding purposes and are not kept from the rest of the body.

5530 EFFECT OF HYPOTHERMIA ON CHANGES IN FINE STRUCTURE IN VILLOUS CELLS OF RAT DUODENUM AFTER LETHAL WHOLE BODY IRRADIATION WITH X-RAYS. *(Ger.)* Bierther, M.; Schluter, G. (Inst. Gen. Exp. Pathol., Bundeswehr, Mainz, Germany). *Strahlentherapie* 145(6):687-701, 1973.

Anesthetized adult Wistar rats were exposed to lethal whole body irradiation (2000-2200 r) with x-rays, to hypothermia (rectal temperature of 8-10° C for 50 min), or to lethal whole body irradiation + hypothermia. The rats were killed 48 hr later, after a 20-hr fast, and tissue slices from the duodenum were examined under the electron microscope. After hypothermia alone, an increase in the number and swelling of Golgi cisterni, many intramitochondrial granules, and glycogen deposits gave evidence of increased metabolic activity. After irradiation alone, 2 types of damaged cells were observed. The first type consisted of light, swollen cells with very marked cytoplasmic damage. In addition to different degrees of mitochondrial swelling, mitochondrial cristae were changed or even lysed. Cisternae of the endoplasmic reticulum and the perinuclear space had disappeared. Ruptures of the apical cell membrane with extrusion of large amounts of cytoplasm into the intestinal lumen were frequently observed. The second type of damaged cells was dark with less marked cytoplasmic changes. Abnormal enlargement of intercellular spaces was characteristic. Less extensive damage occurred in villus cells when rats were irradiated under hypothermia. Autophagic vacuoles and nucleoli formation from endoplasmic reticulum profiles were occasionally observed, while polynuclear cells and fusion between adjacent epithelial cells occurred more often. It is suggested that hypothermia reduces the radiation sensitivity of villus cells appreciably, accounting for the higher survival rates and milder symptoms in animals exposed to radiation while under hypothermia.

5531 CONTRIBUTION OF ELECTRON MICROSCOPY TO SILVER STAIN INTERPRETATION OF ENDOCRINE CELLS IN GASTROINTESTINAL MUCOSA. *(Fr.)* Pradal, G.; L'Hermite, A.; Lefranc, G.; Tusques, J. (Fac. Med., Nantes, France). *Ann. Histochim.* 18(1):19-28, 1973.

Several methods were used to fix fragments of tissue from the stomach, intestine, and cecum of anesthetized rabbits and mice and to impregnate them with silver salts. These specimens were then examined under light or electron microscopes. Preliminary examinations were made on unstained specimens or specimens stained with toluidine blue. Under the light microscope, argentaffinic or argyrophilic cells could be readily distinguished from any other type of endocrine cells by examining semithin slices impregnated with silver salts. After toluidine blue staining, nonimpregnated endocrine cells appeared clear. There were few of these cells in the rabbit fundus, but many appeared in the pylorus (gastrin G cells). Under the electron microscope argentaffinic or argyrophilic cells containing granules of different shapes were most often found in the rabbit cecum. Some of these granules were not impregnated by the method of Fontana or that of Sevier and Munger, but these granules are very osmiophilic and probably argentophilic. If argentaffinic cells have only round granules, they are very difficult to identify under the electron microscope without silver impregnation since they can easily be confused with other types of endocrine cells having round granules. Some round granules in these argentaffinic cells are not impregnated by Fontana's technique. Sevier and Munger's argyrophilic technique makes it possible to identify both typical argentaffinic cells and "EC-L" cells. The latter were not found in the rabbit fundus, as previously reported in the literature, but cells with round granules were found. However, the granules were less intensely impregnated than those of argentaffinic cells. It is difficult to compare these cells with typical argentaffinic cells because of their form and variations in the degree of impregnation. Clear cells observed after toluidine blue staining under the light microscope may be non-impregnated, e.g., A cells from the mouse fundus, D cells from the rabbit fundus, or gastrin cells from the rabbit pylorus. They may also be young ungranulated argentaffinic cells.

5532 HEPATIC ULTRASTRUCTURE IN ENDOTOXEMIA, HEMORRHAGE, AND HYPOXIA: EMPHASIS ON MITOCHONDRIAL CHANGES. *(E.)* White, IV, R. R.; Mela, L.; Bacalzo, Jr., L. V.; Olofsson, K.; Miller, L. D. (Dept. Surg., Univ. Pennsylvania, Philadelphia). *Surgery* 73(4):525-534, 1973.

Electron microscope examinations were made on specimens from the anterior edge and center of livers from male Sprague-Dawley rats with lethal endotoxemia induced by injection of *Escherichia coli* lipopolysaccharide B (5 mg/100 g i.p.). Large, membrane-bound cytoplasmic vacuoles, swollen mitochondria, and abnormal mitochondrial matrices were found in specimens from the edge of the liver. The findings suggest that the vacuoles serve as an intracellular digestive tract in which subcellular organelles are dumped before their destruction by lytic enzymes. Near the center of the liver the shapes of mitochondria differed radically from one hepatocyte to another and even within a single hepatocyte. Degeneration of mitochondrial matrices may be a secondary event. Shock produced by controlled lethal hemorrhages in rats resulted in a great variety of changes in the shapes of mitochondria, but no matrix degeneration or large cytoplasmic vacuoles were observed as in endotoxemia. Findings in both types of shock suggest that the permeability of mitochondrial membranes is changed so that the normal composition of fluid compartments cannot be maintained. Liver mitochondria retained their normal shape in nembutal-anesthetized rats with lethal hypoxia by exposure to nitrogen. However, occasional swollen mitochondrial cristae and slight matrix condensation did occur, indicating increased fluid in the outer compartment intracristal space. This finding was also noted in some mitochondria after both endotoxemia and hemorrhage. The results of this study and a study of the effect of endotoxemia and hemorrhage on mitochondrial respiratory control suggest that hypoxia alone is not responsible for the disintegration of mitochondrial structure and function which occurs in shock.

5533 STUDIES ON THE POSTNATAL GROWTH OF THE LIVER HALVES. *(E.)* Kalbfleisch, H. (Univ. Marburg, Germany). *Beitr. Path. Bd.* 148(3):275-289, 1973.

5534 MICROANGIOGRAPHY OF THE LIVER. *(E.)* Wendelin, H. (Univ. Turku, Finland). *Acta. Paediatr. Scand.* 233:1-58, 1972.

5535 CYTOCHEMICAL ASPECTS OF THE ZYMOGEN IN RAT PANCREAS. ELECTRON MICROSCOPIC STUDY. *(E.)* Ponzo, M.; Rossi, Z.; Picardi, R.; De Filippo, M. G. (2nd Inst. Med. Pathol., Univ. Rome, Italy). *Ann. Histochim.* 18(2):123-129, 1973.

5536 PROTECTIVE EFFECTS OF CYCLOHEXIMIDE AGAINST 1-β-D-ARABINOSYLCYTOSINE-INDUCED INTESTINAL LESIONS. *(E.)* Verbin, R. S.; Diluiso, G.; Farber, E. (Univ. Pittsburgh, Sch. Med., Pa.) *Cancer Res.* 33(9):2086-2093, 1973.

5537 CELL MIGRATION AND THE ALIMENTARY SYSTEM: ENDOCRINE CONTRIBUTIONS OF THE NEURAL CREST TO THE GUT AND ITS DERIVATIVES. *(E.)* Pearse, A. G. E. (Roy. Postgrad. Med. Sch., London, England). *Digestion* 8(4):372-385, 1973.

5538 DISAPPEARANCE OF ACID MUCOPOLYSACCHARIDES FROM THE CELL COATS IN MITOSIS-INDUCED MOUSE LIVER. *(E.)* Ohnishi, T.; Yamamoto, K.; Terayama, H. (Dept. Biol., Tokyo Inst. Tech., Japan). *Histochemie* 36(1):15-20, 1973.

5539 HISTOCHEMICAL CHANGES IN THE FOWL SMALL INTESTINE ASSOCIATED WITH ENHANCED ABSORPTION AFTER FEED RESTRICTION. *(E.)* Michael, E.; Hodges, R. D. (Wye Coll., Ashford, England). *Histochemie* 36(1):39-49, 1973.

5540 GROWTH AND DEVELOPMENT OF NORMAL AND DISEASED GASTROINTESTINAL CELLS. *(E.)* Cooper, M.; Lipkin, M. (Sloan-Kettering Inst. Cancer Res., N.Y., NY.). *Digestion* 8(2):191-200, 1973.

5541 THE ARTERIES OF THE PANCREAS OF THE DOG. AN INJECTION-CORROSION AND MICROANGIOGRAPHIC STUDY. *(E.)* Cadete-Leite, A. (Univ. Luanda, Portuguese West Africa). *Am. J. Anat.* 137(2):151-158, 1973.

5542 COPPER DEFICIENCY IN THE RAT EFFECT ON THE ULTRASTRUCTURE OF HEPATOCYTES. *(E.)*

Gallagher, C. H.; Reeve, V. E.; Wright, R. (Univ. Sydney, Australia). *Australian J. Exp. Biol. Med. Sci.* 51(2):181-189, 1973.

5543 DIFFERENTIATION OF THE MAMMALIAN HEPATIC PRIMORDIUM IN VITRO. I. MORPHOGENESIS AND THE ONSET OF HAEMATOPOIESIS. *(E.)* Johnson, G. R.; Jones, R. O. (Dept. Zool., Univ. Melbourne, Australia). *J. Embryol. Exp. Morphol.* 30(1):83-96, 1973.

5544 STUDIES ON MICROPEROXISOMES. V. ARE MICROPEROXISOMES UBIQUITOUS IN MAMMALIAN CELLS? *(E.)* Novikoff, A. B.; Novikoff, P. M.; David, C.; Quintana, N. (Albert Einstein Coll. Med., Bronx, N.Y.). *Histochem. Cytochem.* 21(8):737-755, 1973.

5545 THE HOMING PATTERN OF THYMUS-DERIVED LYMPHOCYTES IN CALF AND NEONATAL MOUSE PEYER'S PATCHES. *(E.)* Waksman, B. H. (Dept. Microbiol., Yale Univ., New Haven, Conn.). *J. Immunol.* 111(3):878-884, 1973.

5546 MUCOSAL MORPHOLOGY AND CELLULAR RENEWAL IN THE INTESTINE OF CHICKENS FOLLOWING A SINGLE INFECTION OF EIMERIA ACERVULINA. *(E.)* Fernando, M. A.; McCraw, B. M. (Ontario Vet. Coll., Univ. Guelph, Canada). *J. Parasitol.* 59(3):493-501, 1973.

5547 INTRACISTERNAL FIBERS IN THE LIVER CELLS OF STARVED FROGS. *(E.)* Baic, D.; Frye, B. E.; Ladewski, B. G. (Dept. Zool., Univ. Michigan, Ann Arbor). *J. Ultrastruct. Res.* 43(5-6):478-482, 1973.

5548 A HISTOCHEMICAL STUDY OF EPITHELIAL REPAIR OF THE COMMON BILE DUCT IN RATS FOLLOWING MECHANICAL INJURY. *(E.)* Chou, S. T.; Chow, C. W. (Dept. Pathol., Univ. Hong Kong). *Pathology* 5(2):149-161, 1973.

5549 EFFECTS OF STEROIDS UPON THE LIVER ULTRASTRUCTURE. *(E.)* Khandekar, J. D.; Garg, B. D.; Tuchweber, B.; Kovacs, K. (Inst. Med. Exp. Surg. Univ. Montreal, Canada). *Rev. Can. Biol.* 32(2):121-135, 1973.

5550 THE RAMIFICATIONS OF ADRENERGIC NERVE TERMINALS IN THE RECTUM, ANAL SPHINCTER AND ANAL ACCESSORY MUSCLES OF THE GUINEA-PIG. *(E.)* Furness, J. B.; Costa, M. (Dept. Zool., Univ. Melbourne, Australia). *Z. Anat. Entwicklungsgesch.* 140(1):109-128, 1973.

5551 HISTOCHEMICAL ANALYSIS OF MUCOSUBSTANCES IN THE GALLBLADDER EPITHELIUM OF THE DOMESTIC CAT. *(E.)* Varute, A. T.; Nalavade, M. N. (Dept. Zool., Shivaji Univ., Vidyanagar, India). *Folia Histochem. Cytochem.* 11(1):21-32, 1973.

See also, 5568, 5613, 5698.

ABSORPTION–EXCRETION–TRANSPORT

5552 INTESTINAL UPTAKE OF MACROMOLECULES. II. EFFECT OF PARENTERAL IMMUNIZATION. *(E.)* Walker, W. A.; Isselbacher, K. J.; Bloch, K. J. (Massachusetts Gen. Hosp., Boston). *J. Immunol.* 111(1):221-226, 1973.

Female albino Sprague-Dawley rats were parenterally immunized with bovine serum albumin and horseradish peroxidase emulsified in complete Freund's adjuvant. By means of the everted gut sac technique, absorption of these antigens was tested *in vitro*. In rats injected 5 times with bovine serum albumin, uptake of this antigen decreased from 0.36 to 0.17 pmole/mg of mucosal protein in the jejunum and from 0.33 to 0.21 pmole/mg in the ileum. This was not demonstrated in rats injected only twice. Absorption of ^{125}I-horseradish peroxidase and horseradish peroxidase, measured enzymatically, was also significantly inhibited in rats immunized 5 times with horseradish peroxidase. The binding of ^{125}I-bovine serum albumin to intestinal secretions, mucosal extracts, and serum from rats showing interference with bovine serum albumin absorption (multiple injections) was 2- to 10-fold greater than that of comparable preparations from rats which did not show interference (injected twice). Antigen-binding to IgG_a, IgG1, and IgM antibodies was demonstrated by radioimmunoelectrophoresis in the serum of rats with multiple injections of bovine serum albumin; in addition, binding to IgG_a and IgG1 antibodies was demonstrated with mucosal extracts. Although antigen uptake was inhibited in rats immunized parenterally with bovine serum albumin and horseradish peroxidase, the number of gut sacs showing an inhibited response and the extent of the response were less than that previously observed with gut sacs obtained from rats immunized with the same antigens p.o. Binding activity of ^{125}I-bovine serum albumin in mucosal extracts from this latter group of rats was the same as in rats parenterally immunized, but only IgG1 antibodies were noted in mucosal extracts. The more consistent inhibition of antigen uptake in p.o. immunized *versus* parenterally immunized rats may be related to the type or pattern of local antibody distribution.

5553 INFLUENCE OF SODIUM TAUROCHOLATE, CHOLESTYRAMINE, AND MYLANTA ON THE INTESTINAL ABSORPTION OF GLUCOCORTICOIDS IN THE RAT. *(E.)*

Ware, A. J.; Combes, B. (Univ. Texas Southwestern Med. Sch., Dallas). *Gastroenterology* 64(6):1150-1155, 1973.

A micellar solution of sodium taurocholate increased the solubility of cortisol and prednisolone crystals *in vitro*. That this enhanced solubility confers little physiological advantage to the rat was demonstrated in *in vivo* studies on the intestinal absorption of these compounds in adult male Sprague-Dawley rats. Tritiated cortisol and prednisolone crystals were delivered intraduodenally to rats with complete biliary diversion receiving an intraduodenal infusion of 37 mM taurocholate or normal saline. The excretion of the metabolic products of the steroids in bile and urine was used as a measure of the intestinal absorption of the parent compound. Excretion was greater in the first 2 hr after the administration of cortisol or prednisolone in rats receiving bile salts than in bile salt-deficient animals. By 4 hr, however, no significant differences were found in the excretion values between the 2 groups of rats. More than 70% of the administered steroid was recovered in bile and urine within 4 hr in animals with a complete bile-salt deficit. Despite the demonstration, *in vitro*, that both steroid compounds are bound by cholestyramine, no significant decrease in the intestinal absorption of cortisol was observed when cholestyramine or an antacid containing aluminum hydroxide was administered concomitantly. These studies suggest that in a patient with liver disease receiving oral corticosteroid therapy, the absorption of the steroid should not be sufficiently depressed by an intraduodenal bile-salt deficit to interfere with its therapeutic purpose. The concomitant administration of cholestyramine or commercial antacids containing aluminum and magnesium hydroxides would not be expected to interfere significantly with cortisol absorption.

5554 EFFECTS OF 1,25-DIHYDROXYCHOLECALCIFEROL ON INTESTINAL CALCIUM TRANSPORT IN CORTISONE-TREATED RATS. *(E.)*

Favus, M. J.; Walling, M. W.; Kimberg, D. V. (Harvard Med. Sch., Boston, Mass.). *J. Clin. Invest.* 52(7):1680-1685, 1973.

To determine whether the apparent antivitamin activity of steroid hormones is caused by changes in vitamin D metabolism, vitamin-D-deficient control and cortisone-treated (10 mg/day, s.c., for 7 days) rats were injected i.p. with 1,25-dihydroxycholecalciferol (5.5 I.U.), the probable end-organ active vitamin D metabolite in the intestine, and studies of duodenal Ca^{++} transport were performed 16 hr later in modified Ussing chambers. In vitamin D-deficient rats, cortisone administration was associated with a decrease in unidirectional mucosa to serosa flux (J_{MS}), net flux (J_{net}), and the flux ratio (J_{MS}/J_{SM}). While the magnitude of increases in J_{MS} and J_{net} that resulted from 1,25-dihydroxycholecalciferol treatment were about the same in control and cortisone-treated rats, this active vitamin D metabolite failed to restore these parameters to normal levels in cortisone-treated rats. In contrast to results obtained in saline-treated controls, 1,25-dihydroxycholecalciferol failed to reduce the unidirectional serosa to mucosa flux (J_{SM}) in the duodenum of cortisone-treated rats. The cortisone-related defect in Ca^{++} transport was due to changes in both J_{MS} and J_{SM} (decrease in the former and increase in the latter) so that J_{net} and the flux ratio (J_{MS}/J_{SM}) were only about 50% of the levels reached in vitamin D-deficient controls given the same dose of 1,25-dihydroxycholecalciferol. Injection of 1,25-dihydroxycholecalciferol was accompanied by an increase in serum Ca^{++} levels from 1.60 to 2.35 mM, but no response occurred in cortisone-treated rats. Under the experimental conditions employed, the apparent antagonism between glucocorticoids and vitamin D may be due to steroid hormone-related changes in end-organ function. These changes are independent of any direct interaction between the hormone and the vitamin and cannot be reversed by the vitamin.

5555 UPTAKE OF PROTEIN IN SWALLOWED AMNIOTIC FLUID BY MONKEY FETAL INTESTINE IN UTERO. *(E.)*

Lev, R.; Orlic, D. (New York Med. Coll., Valhalla, N.Y.). *Gastroenterology* 65(1):60-68, 1973.

Horseradish peroxidase (500 mg), was injected into the amniotic sac of 4 pregnant monkeys. The actual dose of the enzyme determined after the amount of amniotic fluid could be measured ranged from 4.1 to 10 mg/cc amniotic fluid. After 7 hr, segments of fetal small intestine were fixed, sectioned, and incubated for peroxidase in a diaminobenzidine-hydrogen peroxide medium. Light and electron microscopic examination revealed peroxidase uptake in 3 animals, 2 of which represented term fetuses and 1 a middle trimester fetus. The predominance of the enzyme in the proximal intestine of the younger fetus is attributed to underdevelopment of fetal swallowing and intestinal transit at this age. Absorbed peroxidase granules were most abundant in cells lining the upper regions of the villi and were found throughout the cytoplasm of the apical half of the cells. Frozen sections incubated for both acid phosphatase and peroxidase revealed a superimposed reaction for both enzymes in the cell apex, suggesting that at least part of the incorporated peroxidase is degraded by lysosomes. Thus, the monkey fetal intestine has the capacity to take up macromolecular protein contained within swallowed amniotic fluid. It may prove feasible to introduce compounds beneficial to the developing human fetus *via* the amniotic fluid, e.g., antigens might be injected to investigate the immunological potential of fetal intestinal or peripheral lymphoid tissues, thus avoiding the need to perform open surgery to expose the fetus.

5556 THE INFLUENCE OF SECRETIN ON ION TRANSPORT IN THE HUMAN JEJUNUM. *(E.)* Hicks, T.; Turnberg, L. A. (Royal Infirm., Manchester, England). *Gut* 14(6):485-490, 1973.

By using a triple-lumen tube perfusion technique in 37 normal human subjects (aged 18-40 yr), secretin (2U/kg/hr, i.v.) was shown to reduce the absorption of sodium, potassium, and chloride ions and water in the most proximal 30 cm of jejunum but to have no effect on bicarbonate absorption. This effect was not due to an artefact produced by the entry of secretin-stimulated, bicarbonate-rich pancreatic juice into the test segment. Absorption of sodium chloride and water was stimulated rather than inhibited by higher bicarbonate concentrations and the effect of secretin was obvious even when this factor was controlled by adjusting the bicarbonate concentrations of the test fluids. Secretin did not influence ion transport in the mid-jejunum. It has been proposed that the effect of secretin was produced by stimulation of Brunner's glands secretion. However, it does not seem likely that these glands are present in the jejunum in sufficient numbers to produce all the effects observed in these experiments. The effects described may indicate a physiological role for secretin in the intestine, where it could prevent too rapid dehydration of upper jejunal contents, which might interfere with adequate mixing and digestion.

5557 RECEPTORS FOR VITAMIN B_{12} RELATED TO ILEAL SURFACE AREA AND ABSORPTIVE CAPACITY. *(E.)* Donaldson, Jr., R. M.; Small, D. M.; Robins, S.; Mathan, V. I. (Boston Univ. Sch. Med., Mass.). *Biochim. Biophys. Acta* 311(3):477-481, 1973.

Isolated microvillous membranes from hamster ileum bind *in vitro* 1.4 x 10^{-12} mol of intrinsic factor-vitamin B_{12} complex. The maximum absorption from a single dose of vitamin B_{12} *in vivo* was found to be about 3 times as great (4 x 10^{-12} mol). The limited number of intrinsic factor-vitamin B_{12} receptor sites (8.5 x 10^{11}/hamster ileum) are distributed over approximately 7000 cm^2 of ileal surface area, corresponding to less than one receptor/microvillus. The extremely slow rate of absorption of vitamin B_{12} observed *in vivo* suggests prolonged interaction between intrinsic factor-vitamin B_{12} complex and the membrane receptor.

5558 INTESTINAL CALCIUM TRANSPORT: STIMULATION BY LOW PHOSPHORUS DIETS. *(E.)* Tanaka, Y.; Frank, H.; DeLuca, H. F. (Dept. Biochem., Univ. Wisconsin, Madison). *Science* 181(4099):564-566, 1973.

Male rats from a low vitamin D colony were maintained on a vitamin D-deficient diet containing 1.2% calcium and 0.1 or 0.3% phosphorus for 4 weeks. For each concentration of phosphorus, a third of the rats received 130 pmole daily of nonradioactive 25-hydroxyvitamin D_3, p.o. in 0.1 ml of cottonseed-soybean oil, for the last 2 weeks. Another third received 130 pmole tritiated 25-hydroxyvitamin D_3 while the remaining third received the 0.1 ml of oil vehicle daily during the last 2 weeks. Rats receiving the oil or the nonradioactive vitamin were used to measure intestinal calcium transport by the everted sac method. The low phosphorus diet produced severe hypophosphatemia that was partly corrected by the 25-hydroxyvitamin D_3 treatment. Animals on this diet exhibited marked intestinal calcim transport activity. Rats fed normal phosphorus amounts showed a hypophosphatemia that was corrected by the 25-hydroxyvitamin D_3 treatment. These rats had calcium transport about half that of rats on the low phosphorus diet. The low phosphorus diet and the resulting hypophosphatemia stimulated 1,25-hydroxyvitamin D_3 production which, it is suggested, caused the increased calcium transport and contributed further to the hypercalcemia. The increased accumulation of 1,25-hydroxyvitamin D_3 under the hypercalcemia and hypophosphatemia conditions demonstrates that parathyroid hormone is not needed for 1,25-hydroxyvitamin D_3 production in the hypophosphatemic animal. The suggestion that inorganic phosphate concentration in renal cells is important in 1,25-hydroxyvitamin D_3 production is also supported by these results.

5559 EFFECTS OF ANTIBIOTICS AND OTHER AGENTS ON THE INTESTINAL TRANSPORT OF IRON. *(E.)* Greenberger, N. J. (Univ. Kansas Med. Ctr., Kansas City). *Am. J. Clin. Nutr.* 26(1):104-112, 1973.

To determine whether the previously reported development of iron- deficiency anemia in erythropoietic protoporphyria patients treated on a long-term basis with cholestyramine may have been due to an intraluminal binding of iron by the drug, *in vitro* and *in vivo* studies were carried out to characterize the effects of cholestyramine on the intestinal transport of inorganic and hemoglobin iron in the rat. It was found that cholestyramine bound appreciable amounts of inorganic and hemoglobin iron *in vitro*; the binding of inorganic iron was less obviously pH dependent than organic iron; cholestyramine treatment impaired the intestinal absoprtion of inorganic iron in normal bled, and iron-loaded rats; cholestyramine treatment diminished the intestinal absorption of hemoglobin iron in bled rats; and cholestyramine treatment for 6 months resulted in significantly decreased non-heme iron stores in the spleen, liver, and intestinal mucosa in the rat. These studies emphazied the importance of drug-drug and drug-nutrient interrelationships in the gut lumen, and served to show that certain drugs can significantly affect the absorption of nonrelated compounds. These studies also raised the important question as to whether long-term administration of cholestyramine to patients with a variety of disorders will result in the development of occult iron-deficiency anemia. In this regard, particular attention should be directed toward patients with problems such as uremia, hypermenorrhea, and gastric achlorhydria because a cholestyramine-induced slight decrease in iron absorption in such patients might well be more significant than in healthy individuals.

5560 EVIDENCE FOR HORMONAL REGULATION OF INTESTINAL ABSORPTION BY CHOLECYSTOKININ. *(E.)* Bussjaeger, L. J.; Johnson, L. R. (Health Sci. Ctr., Univ. Oklahoma, Oklahoma City). *Am. J. Physiol.* 224(6):1276-1279, 1973.

The effect of cholecystokinin on intestinal absorption was studied by measuring the amount of fluid, glucose, and electrolytes remaining in canine jejunal and ileal loops after a 15-min exposure to a known amount of Krebs-Ringer-bicarbonate buffer. Experiments lasted 3 hr and consisted of a middle test hr, during which cholecystokinin was infused i.v. or fat was instilled in the duodenum, bracketed by 2 hr during which saline was infused i.v. Exogenous cholecystokinin (4 U/kg/hr) inhibited the absorption of fluid, Na, K, and Cl in both the jejunal and ileal loops. In the jejunal loop cholecystokinin significantly increased the absorption of glucose from 68.02 to 75.34 mg after 2 hr. Cholecystokinin induced secretion of bicarbonate in the ileum, for more bicarbonate was recovered than instilled. Instillation of fat in the duodenal-jejunal portion of the bowel duplicated the effects of exogenous cholecystokinin on the ileal loop. These studies indicate that cholecystokinin inhibits the absorption of fluid and electrolytes from the small intestine, and enhances glucose uptake slightly in the jejunum. These effects of cholecystokinin appear to be physiological. It is suggested that cholecystokinin and gastrin retard the absorption of water in order to insure sufficient volume for mixing, enzyme digestion, solubilization, and absorption of foodstuffs, especially fat. The observation that cholecystokinin did not inhibit glucose absorption, but actually stimulated it, supports this view.

5561 THE RETENTION AND MOVEMENT OF CERIUM-141 IN THE GASTROINTESTINAL TRACT OF ADULT RATS IRRADIATED WITH 800 R AND FED GRAIN-BASED OR MILK DIETS. *(E.)* Sagan, C. E.; Lengemann, F. W. (New York State Vet. Coll., Ithaca). *Radiat. Res.* 53(3):480-487, 1973.

Mature male albino rats (Blue Spruce) were used to determine the effect of 800 R of gamma irradiation on the retention of ^{141}Ce when the animals were either fasted, fed a commercial rat diet, or fed liquid cows milk. In addition, a study was carried out to determine the rate of transit of ^{141}Ce through the small intestine of normal and irradiated rats. Radiation slowed the transit of radiocerium through the small intestine and had a greater effect upon the stomach, upper, and midjejunum than it did on the other segments. Thus, intestinal transport rates for the movement of ^{141}Ce through the duodenum, jejunum, jejunum-ileum, and ileum in normal rats were 153, 85, 20, and 11 cm/hr, resp., while in irradiated rats these values change to 65, 15, 11, and 7 cm/hr, resp. Radiation did not, however, lead to a significant increase in permeability of the intestine for cerium. This was contrary to observations with strontium and calcium, but possibly explained by the fact that cerium can polymerize, form colloids, or interact with proteins to form products with low rates of transport across biological barriers while strontium and calcium tend to remain as cations of small dimensions. Fasting also did not produce a significant uptake of radiocerium into the body but increased, somewhat, the passage of the radionuclide through the tract. Milk feeding, on the other hand, markedly slowed the movement of radiocerium through the gut and produced some increase in the absorption of radiocerium into the body. For example, at 7 days after dosing, the milk-fed animals retained about 6-8 times more radiocerium than corresponding rats fed the commercial diet. There exists, therefore, the possibility that absorption of cerium may be improved by milk feeding.

5562 CHARACTERISTICS OF AMINO ACID ACCUMULATION BY ISOLATED INTESTINAL EPITHELIAL CELLS. *(E.)* Tucker, A. M.; Kimmich, G. A. (Sch. Med. Dent., Univ. Rochester, N.Y.). *J. Membrane Biol.* 12:1-22, 1973.

Accumulation of neutral amino acids by isolated chick epithelial cells was studied. The cells establish 4- to 8-fold concentration gradients of amino acids at an extracellular concentration of 1 mM. The accumulation is sodium-dependent, inhibited by high extracellular potassium concentrations, and is sensitive to a variety of metabolic inhibitors. Also, amino acid uptake is depressed by actively transported sugars and certain other amino acids and is stimulated by 200 μM phloridzin. Cells equilibrated with valine and loaded with 30-40 mM intracellular sodium begin immediately to actively accumulate valine when suddenly introduced to media containing 20 mM sodium. The cells establish a 3-fold gradient of amino acid during the interval when intracellular sodium is higher than extracellular sodium. Amino acid accumulation and ^{22}Na efflux were monitored simultaneously in cells treated with phloridzin. While phloridzin causes a 30% stimulation of amino acid uptake, no variation in the rate of ^{22}Na efflux or the steady-state level of ^{22}Na maintained by the cells can be detected. Similarly, 2.5 mM glucose or 2.5 mM 3-O-methylglucose cause approximately a 50% inhibition of 1 mM valine uptake but no detectable change in steady-state cellular ^{22}Na content. Several aspects of the data seem inconsistent with concepts embodied in the ion gradient hypothesis, and it is suggested that a directly energized transport mechanism can better accommodate all of the data.

5563 ZINC METABOLISM IN THE RAT. I. INTESTINAL ABSORPTION OF ZINC. *(E.)* Methfessel, A. H.; Spencer, H. (VA Hosp., Hines, Ill.). *J. Appl. Physiol.* 34(1):58-62, 1973.

Studies were conducted to determine changes in intestinal absorption of ^{65}Zn with time in intact male albino Sprague-Dawley rats and to compare this absorption with that from specific intestinal sites isolated by the formation of *in vivo* ligated intestinal sacs. The intestinal absorption of ^{65}Zn in the intact rat was rather rapid attaining a maximum of about 25% ^{65}Zn within 30 min after the intubation of the radioisotope. This level of ^{65}Zn absorption was maintained over the next 7.5 hr and then decreased. Similar intestinal absorption rates were observed when the ^{65}Zn was instilled into *in vivo* ligated sacs formed from the duodenal portion of the small intestine. The absorption of ^{65}Zn was significantly greater from the duodenum than from more distal portions of the small intestine. The absorption of ^{65}Zn was slightly greater from the midjejunum than from the ileum but the difference was not statistically significant. Only minimal amounts of ^{65}Zn were absorbed from the stomach, the cecum, and the colon. It is felt that the large muscle mass may represent a considerable reservoir for endogenous zinc in the rat. The liver and pancreas stored considerable amounts of ^{65}Zn with peak levels occurring in 3 hr for the liver and 4 hr for the pancreas. The turnover rate in liver and pancreas was rapid and these tissues exhibited a significant decrease in ^{65}Zn concentration at 24 hr.

5564 DETERMINANTS OF INTESTINAL MUCOSAL UPTAKE OF SHORT- AND MEDIUM-CHAIN FATTY ACIDS AND ALCOHOLS. *(E.)* Sallee, V. L.; Dietschy, J. M. (Univ. Texas Southwestern Med. Sch., Dallas). *J. Lipid Res.* 14(4):475-484, 1973.

Uptake rates across the jejunal brush border in rats were measured for water-soluble fatty acids and alcohols. The relative roles of the unstirred water layer and the lipid cell membrane as determinants of the intestinal absorptive process were studied. Initial measurements of time courses of electrical transients developed across the intestine exposed to poorly permeant solute molecules showed no anomalous discrimination of probe molecules of different size or charge. Thus, the diffusion barrier in the intestine can be considered as an unstirred water layer. Uptake rates of fatty acid were linear with respect to concentration of the test solute, demonstrated no competitive inhibition of contralateral stimulation, had low temperature dependency, and were insensitive to metabolic inhibition, indicating that uptake proceeds by passive diffusion. Passive permeability coefficients varied from 22 to 395 nmoles/min/100/mg/mM for the saturated fatty acids 2:0 through 12:0 and from 119 to 581 for the saturated alcohols 6:0 through 10:0. Vigorous stirring of the bulk buffer solution enhanced permeability coefficients in direct proportion to chain length. However, the presence of bile acid micelles depressed apparent permeability coefficients in proportion to fatty acid chain length. These results demonstrate that uptake of short-chain fatty acid monomers is rate limited by the lipid cell membrane but diffusion through the unstirred water layer becomes increasingly rate limiting as the chain length increases. It is also possible to conclude that diffusion through the unstirred water layer becomes totally rate limiting for uptake of long-chain fatty acid monomers of physiological importance.

5565 STUDIES ON THE TRANSPORT OF GLUCOSE FROM DISACCHARIDES BY HAMSTER SMALL INTESTINE IN VITRO. I. EVIDENCE FOR A DISACCHARIDASE-RELATED TRANSPORT SYSTEM. *(E.)* Malathi, P.; Ramaswamy, K.; Caspary, W. F.; Crane, R. K. (Rutgers Med. Sch., Piscataway, N.J.). *Biochim. Biophys. Acta* 307(3): 613-626, 1973.

When disaccharides were incubated with rings from everted hamster small intestine in the presence of saturating concentrations of free D-glucose (30-100 mM), total glucose uptake was enhanced beyond the theoretical V for free glucose uptake. This phenomenon did not occur when glucose-1-phosphate was the substrate. Galactose and β-methyl glucoside, analogs of the D-glucose transport system, inhibited glucose uptake from sucrose. In turn, the uptake of galactose and β-methyl glucoside was inhibited noncompetitively by disaccharides. Phlorizine inhibited glucose uptake from sucrose competitively at low concentrations and noncompetitively at high concentrations. Sucrose did not induce counterflow of preloaded β-methyl glucoside. These findings indicate that there is a disaccharidase-related component of monosaccharide transport which is present in addition to and is different from the Na$^+$-dependent glucose transport system.

5566 INTESTINAL ABSORPTION OF SUCROSE. *(E.)* Dahlqvist, A. (Univ. Hosp., Lund, Sweden). *Acta Med. Scand. (Suppl.)* 542:13-18, 1972.

5567 ACCELERATION OF EXCHANGE OF Na+ FOR H+ ACROSS GASTRIC MUCOSA BY SHORT-CHAIN FATTY ACIDS. *(E.)* Ventura, U. L.; Schlegel, J. F.; La Force, R. C.; Code, C. F. (Mayo Clin., Rochester, Minn.). *Am. J. Physiol.* 225(1):33-37, 1973.

5568 MECHLORETHAMINE EFFECTS ON INTESTINAL ABSORPTION IN VITRO AND ON CELL PROLIFERATION. *(E.)* Wurth, M. A.; Musacchia, X. J. (Dalton Res. Ctr., Univ. Missouri, Columbia). *Am. J. Physiol.* 225(1):73-80, 1973.

5569 REGULATION OF CALCIUM ABSORPTION BY FOWL INTESTINE. *(E.)* Hurwitz, S.; Bar, A.; Cohen, I. (Inst. Anim. Sci., Volcani Ctr., Bet Dagan, Israel. *Am. J. Physiol.* 225(1):150-154, 1973.

5570 EFFECT OF CORTICOSTEROIDS ON INTESTINAL IRON ABSORPTION. *(It.)* Tamburino, G.; Lombardo, G. (Inst. Med. Semeiotics, Univ. Catania, Italy). *Haematol. Arch.* 56(11/12):559-562, 1971.

5571 PURINE NUCLEOTIDE ENTRY, EXIT, AND INTERCONVERSIONS IN BULLFROG GASTRIC MUCOSA. *(E.)* Kidder, G. W. (Wesleyan Univ., Middletown, Conn.). *J. Appl. Physiol.* 224(4):809-817, 1973.

5572 SODIUM-DEPENDENT SUGAR TRANSPORT IN THE INTESTINE. *(E.)* Goldner, A. M. (Univ. California Med. Sch., Davis). *Metabolism* 22(5): 649-656, 1973.

5573 CALCITONIN INHIBITION OF INTESTINAL PHOSPHATE ABSORPTION. *(E.)* Tanzer, F. S.; Navia, J. M. (Fac. Dent., Univ. Alabama, Birmingham). *Nature (New Biol.)* 242(120):221-222, 1973.

5574 HOMEOSTATIC REGULATION OF ZINC ABSORPTION IN THE RAT. *(E.)* Evans, G. W.; Grace, C. I.; Hahn, C. (Human Nutr. Res. Lab., USDA, Grand Forks, N.D.). *Proc. Soc. Exp. Biol. Med.* 143(3): 723-725, 1973.

See also, 5539, 5865, 5933.

MOTILITY

5575 ELECTRICAL STIMULATION OF GASTRIC ELECTRICAL CONTROL ACTIVITY. *(E.)* Sarna, S. K.; Daniel, E. E. (Dept. Electr. Eng. Pharmacol., Univ. Alberta, Edmonton, Canada). *Am. J. Physiol.* 225(1): 125-131, 1973.

Voltage pulses of 100 msec duration and 1- to 25-V amplitude were used to stimulate gastric electrical control activity in anesthetized dogs. The gastric control waves could be entrained from any site in the electrically active region on the anterior and posterior sides. The maximum frequency at which the gastric control waves could be entrained by the electronic pacemaker varied from dog to dog. Mean maximum driven frequency was 6.98 cycles/ min. The strength of stimulus required to entrain gastric control waves increased for larger differences between the driven frequency and the natural frequency of gastric control waves. Total phase lag between control waves in the corpus and in the antrum increased when the control waves were driven at a frequency higher than their natural frequency. The stomach was divided into 3 segments by circumferential cuts in muscle layers. The proximal segment that contained the highest intrinsic frequency oscillator had the least maximum driven frequency (mean 6.92 cycles/ min). The mean maximum driven frequency increased distally (middle segment mean maximum driven frequency, 7.55 cycles/min; distal segment mean maximum driven frequency, 7.74 cycles/min). Physostigmine (20-60 μg/kg i.v.) decreased the maximum driven frequency of the distal segment, whereas atropine (5-20 μg/kg, i.v.) increased its maximum driven frequency. These drugs, in particular physostigmine, had a small effect on the maximum driven frequency of the middle segment and very little or no effect on the maximum driven frequency of the proximal segment. This study confirms that a system of bidirectionally coupled relaxation oscillators can account for more characteristics of the gastrointestinal electrical control activity than a relaxation oscillator model with only forward coupling or a cable model. The study also shows that nerves could be important in determining some of the characteristics of gastric relaxation oscillators, such as their ability to be driven by electronic pacemakers.

5576 EFFECT OF A NEW ANTICHOLINERGIC AGENT (SA-504) ON MOTILITY OF THE GASTROINTESTINAL TRACT AND THE URINARY BLADDER IN CATS. *(E.)* Tamaki, H.; Ikeo, T.; Harigaya, S.; Nakajima, H. (Biol. Res. Lab., Tanabe Seiyaku Co., Saitama, Japan). *Jap. J. Pharmacol.* 23(3):391-400, 1973.

5577 MEMBRANE-ASSOCIATED PARTICLES: INCREASE AT SITES OF PINOCYTOSIS DEMONSTRATED BY FREEZE-ETCHING. *(E.)* Orci, L.; Perrelet, A. (Sch. Med., Univ. Geneva, Switzerland). *Science* 181(4102): 868-869, 1973.

5578 EFFECT OF VAGOTOMY ON THE PYLORIC SPHINCTER IN THE RAT. *(It.)* Munari, P. F.; Cordioli, G. P.; Bernardi, R. (Inst. Normal Human Anat., Univ. Padua, Italy). *Boll. Soc. Ital. Biol. Sper.* 48(21): 700-705, 1972.

5579 AN IMPROVED METHOD FOR STUDYING PERISTALSIS IN THE ISOLATED GUINEA PIG ILEUM. *(E.)* Van Nueten, J. M.; Geivers, H.; Fontaine, J.; Janssen, P. A. J. (Janssen Pharmaceutica, Beerse, Belgium). *Arch. Int. Pharmacodyn.* 203(2):411-414, 1973.

5580 THE MYENTERIC PLEXUS IN THE OESOPHAGUS OF THE TOAD (BUFO MELANOSTICTUS). *(E.)* Wong, W. C. (Dept. Anat., Univ. Singapore). *Acta Anat.* 85(1):52-62, 1973.

5581 MECHANICAL PROPERTIES OF GUINEA PIG TAENIA COLI MUSCLES. *(E.)* Lowy, J.; Mulvany, M. J. (Biophys. Inst., Aarhus Univ., Denmark). *Acta Physiol. Scand.* 88(1):123-136, 1973.

5582 EFFECTS OF CAFFEINE ON ELECTRICAL AND MECHANICAL ACTIVITIES OF GUINEA PIG TAENIA COLI. *(E.)* Sunano, S.; Miyazaki, E. (Sapporo Med. Coll., Japan). *Am. J. Physiol.* 225(2):335-339, 1973.

5583 THE STOMACH MOTOR-EVACUATORY ACTIVITY IN CASE OF DISTURBANCE OF ITS BLOOD SUPPLY. *(Rus.)* Korotko, G. F.; Aripov, A. N.; Ustinov, V. A (Med. Inst., Andijan, USSR). *Fiziol. Zh. SSSR* 59(7):1058-1063, 1973.

5584 ON THE SPEED OF PASSAGE OF THE PROXIMAL SMALL INTESTINE CONTENTS IN DOGS. *(Rus.)* Bogatch, P. G.; Gubkin, V. A.; Groisman, S. D. (T. H. Shevchenko Inst. Physiol. State Univ., Kiev, USSR). *Fiziol. Zh. SSSR* 59(7):1081-1086, 1973.

5585 INERTIA AND STREAMLINE CURVATURE EFFECTS ON PERISTALTIC PUMPING. *(E.)* Jaffrin, M. Y. (Massachussetts Inst. Technol., Cambridge). *Int. J. Engng. Sci.* 11(6):681-699, 1973.

See also, 5561, 5807, 5871, 5879.

SECRETION AND METABOLISM

5586 SECRETION AND TRANSDUCTAL FLUXES OF IONS IN EXOCRINE GLANDS OF THE MOUSE. *(E.)* Mangos, J. A.; McSherry, N. R.; Nousia-Arvanitakis, S.; Irwin, K. (Univ. Wisconsin Med. Sch., Madison). *Am. J. Physiol.* 225(1):18-24, 1973.

Micropuncture, microperfusion, and microanalytical techniques were used to study the secretory mechanisms and transductal fluxes of water and monovalent ions were investigated in the parotid, submaxillary, and pancreas of the male Swiss-Webster mouse. The osmolarity and the concentrations of monovalent ions of the fluid obtained from the intercalated ducts of the salivary glands during stimulation with pilocarpine (0.01 mg/10g, i.v.) were similar to or slightly higher than those observed in the mouse plasma, and they did not change with changes in the flow rate. Salivary hypotonicity was produced by net efflux of sodium and chloride in excess of water in the intralobular ducts of the glands while net transductal influx of small amounts of potassium took place. These transductal events resulted in the observed, flow rate-dependent changes in the composition of the respective salivas. In the pilocarpine- or secretin (0.10 μ/min, i.v. infusion)-stimulated mouse pancreas, the acinar fluid was isotonic or slightly hypertonic to plasma with high chloride and low bicarbonate concentrations as in the rat pancreas. No net transductal fluxes of anions took place during either form of secretory stimulation, and the ionic composition of the final pancreatic juice was identical to that of the primary secretory (acinar) fluid. Simultaneous measurements of amylase concentrations in the primary fluid and final product of parotid and pancreas and *in situ* microperfusion of the main submaxillary duct, demonstrated that the duct systems of these glands are impermeable to water. These results suggest that in these 3 exocrine glands of the mouse, the secretory process is active transacinar transport of electrolytes.

5587 THE EFFECTS OF CHANGES IN ARTERIAL PLASMA CLACIUM CONCENTRATION ON SUBMANDIBULAR SECRETORY POTENTIALS. *(E.)* Creed, K. E.; McDonald, I. R. (Monash Univ., Clayton, Australia). *J. Physiol.* 231(2):327-340, 1973.

5588 ACTION OF DRUGS ON DENERVATED MYOEPITHELIAL CELLS OF SALIVARY GLANDS. *(E.)* Emmelin, N.; Thulin, A. (Univ. Lund, Sweden). *Br. J. Pharmac.* 48(1):73-79, 1973.

5589 METABOLIC TURNOVER OF SULPHATED HETEROGLYCANS IN THE GASTROINTESTINAL TRACT, CARTILAGE AND SKIN OF THE RAT. *(E.)* Terho, T. T.; Hartiala, K. (Univ. Turku, Finland). *Biochem. Biophys. Acta.* 304(3):591-610, 1973.

5590 CYCLIC AMP IN DIGESTIVE PHYSIOLOGY. *(E.)* Levine, R. A. (Upstate Med. Ctr., Syracuse, N.Y.). *Am. J. Clin. Nutr.* 26(8):876-881, 1973.

5591 AUTORADIOGRAPHY. FUNCTIONAL HISTOCHEMICAL INVESTIGATION OF THE DIGESTIVE MUCOSA. *(Fr.)* Bescol-Liversac, J.; Guillam, C. (Fernand-Widal Hosp., Paris, France). *Ann. Anat. Pathol. (Paris)* 17(3):279-306, 1972.

5592 THE EFFECT OF CORTICOSTERONE ON EXTRANEURONAL AMINE UPTAKE AND EFFECTOR RESPONSE IN RAT SALIVARY GLANDS. *(E.)* Almgren, O.; Jonason, J. (Dept. Pharmacol., Univ. Goteborg, Sweden). *J. Pharm. Pharmacol.* 25(7):537-543, 1973.

5593 GALACTOSE ELIMINATION CAPACITY IN THE RAT. *(E.)* Keiding, S. (Rigshosp., Copenhagen, Denmark). *Scand. J. Clin. Lab. Invest.* 31(3):319-325, 1973.

5594 LACTOSE AND CALCIUM METABOLISM: A REVIEW. *(E.)* Ali, R.; Evans, J. L. (Rutgers Univ., New Brunswick, N.J.). *J. Agric. Univ. Puerto Rico* 57(2):149-164, 1973.

SECRETION AND METABOLISM

Stomach

5595 THE METABOLIC CLEARANCE RATE AND HALF-LIFE OF SYNTHETIC HUMAN GASTRIN IN DOGS. *(E.)* Schrumpf, E.; Semb, L. S. (Aker Hosp., Oslo, Norway). *Scand. J. Gastroenterol.* 8(3):203-207, 1973.

Synthetic human gastrin (1 μg/kg) was infused at a constant rate of 10.2 ml/hr for 2 hr in dogs. The gastrin level was determined by radioimmunoassay in plasma samples before, during, and at frequent intervals after the infusion. The gastric acid output from a Heidenhain pouch was also measured. During infusion the gastrin concentration and gastric acid output reached a plateau level. A rapid decline in the plasma concentration of gastrin was observed after the infusion was stopped. Regression analysis indicated that the disappearance curve fits best a single exponential, suggesting that gastrin removal is directly proportional to its concentration. The mean metabolic clearance rate was 70 ml/min/kg. The mean half-life of gastrin was 3.7 min. The mean plateau blood level, half-life, and metabolic clearance rate of gastrin were not influenced by simultaneous infusion of secretin. Because the metabolic clearance rate exceeds renal plus splanchnic blood flow, it is suggested that gastrin is metabolized also outside the splanchnic and renal region.

5596 GASTRIC SECRETION OF PEPSIN IN PATIENTS WITH PRIMARY HYPERPARATHYROIDISM BEFORE AND AFTER REMOVAL OF PARATHYROID ADENOMAS. *(E.)* Christiansen, J. (Rigshospital, Copenhagen, Denmark). *Scand. J. Gastroenterol.* 31(3):337-340, 1973.

Gastric secretion of pepsin was studied in 7 patients (2 men and 5 women, aged 46-63 yr) before and after removal of parathyroid adenomas. No changes in basal pepsin secretion were found. However, the pepsin secretion during stimulation with histamine (42 μg/kg/hr, i.v., for 90 min) was significantly reduced after removal of the parathyroid adenomas. Regression analysis seems to indicate a relation between the altered serum calcium concentration and the altered gastric secretory capacity of pepsin. Several possible explanations for this relation exist. Calcium may act on pepsin secretion through release of gastrin, a mechanism in which cyclic-AMP may be involved. It is also suggested that the reduced pepsin secretion after removal of parathyroid adenomas is caused by the reduced concentration of parathyroid hormone which in turn reduces the concentration of cyclic-AMP and that the relation to serum calcium only reflects the alteration in concentration of parathyroid hormone. The results of the present study supports the hypothesis that the higher secretory capacity of pepsin may be an ulcerogenetic factor in the hyperparathyroid condition.

5597 EFFECT OF PARTLY PURIFIED GASTRONE ON ACID SECRETION, BODY TEMPERATURE, AND LEUKOCYTE COUNT IN THE DOG. *(E.)* Cowley, D. J. (Univ. Hosp. South Manchester, England). *Gastroenterology* 65(1):43-53, 1973.

Partly purified gastrone extracted from human achlorhydric gastric juice was assayed in 3 dogs with vagally denervated (Heidenhain) or in 3 other dogs with vagally innervated (Pavlov) gastric pouches. Assays with histamine, administered either as a single, s.c.

injection at 3 1-hr intervals, or by continuous i.v. infusion, showed that inhibition of hydrochloric acid secretion by gastrone was dose-related. The dose of gastrone inhibiting secretion by 50% (inhibited dose 50), was between 55-100 µg. In the dogs with vagally innervated pouches, assays with a standard 100-cal meat meal were performed. Dose-responsive inhibition of secretion was observed with an inhibited dose 50 of 10-30 µg. Pyrexia was induced by gastrone in 60 of 64 assays. The rectal temperature increased significantly during the 1st hr, peaked at 2 hr, and then decreased. Inhibition of secretion followed a parallel course, but lagged 1 hr behind pyrexia. In 4 of the meat meal assays, using 0.5 and 1.0 µg/kg of gastrone, secretion was inhibited -24% and -45%, resp., without a temperature rise. Gastrone induced an initial leukopenia, followed by a leukocytosis. The pooled achlorhydric gastric juice from which the gastrone was prepared contained a mixed group of oral commensal bacteria. Gastrone and bacterial endotoxins produce similar effects on gastric acid secretion, body temperature, and leukocyte levels and the time course of these effects is also similar.

5598 STIMULATION OF GASTRIC ACID SECRETION BY 5-METHYL HISTAMINE IN CAT. *(E.)* Impicciatore, M.; Grossman, M. I. (VA Wadsworth Hosp. Ctr., Los Angeles, Calif.). *Am. J. Dig. Dis.* 18(7):551-555, 1973.

Histamine and 5-methyl histamine were used to study gastric secretion in cats in which permanently installed plastic cannulas had been used to form gastric fistulas. Each drug was infused at concentrations ranging from 10-640 µg/kg/hr, i.v. After histamine infusion had ceased, secretion returned to basal levels within 40 min. However, secretion stimulated by 5-methyl histamine continued for as long as 6 hr, dropping gradually to basal levels, probably reflecting a slower degradation rate for this drug. The maximum response was greater with 5-methyl histamine than with histamine. Whether all doses were given within 30 min of each other, or given on successive days, made little difference to the calculated maximal responses to either drug. The D_{50} of histamine was the same with either mode of administration. However, the D_{50} of 5-methyl histamine was significantly greater when the drug was administered at 30 min intervals than when administered on successive days. It is suggested that the D_{50} of 5-methyl histamine derived from the 1 dose/day study is probably the more meaningful value to use in estimating the relative potency of the 2 drugs. Using the ratio of D_{50}'s as an estimate of relative potency, 5-methyl histamine was 1.8 times more potent than histamine. It is strongly suggested that this greater response with serial doses than with 1 dose/day studies is a true species difference, i.e., peculiar to cats and to the drug.

5599 ISOLATION OF GASTRIC VITAMIN B_{12}-BINDING PROTEINS USING AFFINITY CHROMATOGRAPHY. II. PURIFICATION AND PROPERTIES OF HOG INTRINSIC FACTOR AND HOG NONINTRINSIC FACTOR. *(E.)* Allen, R. H.; Mehlman, C. S. (Washington Univ. Sch. Med., St. Louis, Mo.). *J. Biol. Chem.* 248(10):3670-3680, 1973.

Two vitamin B_{12}-binding proteins, hog intrinsic factor and hog nonintrinsic factor, have been isolated from hog gastric mucosa. Affinity chromatography on vitamin B_{12}-Sepharose removed the bulk of protein from a crude extract of hog gastric mucosa. The two vitamin B_{12}-binding proteins were separated subsequently by selective affinity chromatography with an affinity adsorbent containing covalently bound derivatives of vitamin B_{12} that lack the nucleotide portion of the native vitamin. Hog nonintrinsic factor was absorbed to a column of this material; hog intrinsic factor was not. After additional purification both proteins were isolated in homogeneous form based on polyacrylamide disc gel electrophoresis, sedimentation equilibrium ultracentrifugation, and sodium dodecyl sulfate polyacrylamide gel electrophoresis. Hog intrinsic factor (24 µg) corrected vitamin B_{12} malabsorption when given to a patient with pernicious anemia. Hog nonintrinsic factor (49 µg) had no effect. Hog intrinsic factor binds 30.3 µg of vitamin B_{12}/mg of protein. Molecular weights of 52,300 to 58,600 were obtained. The protein contains 17.5% carbohydrate. In the presence of vitamin B_{12} hog intrinsic factor aggregates to form dimers and higher molecular weight oligomers. Hog nonintrinsic factor binds 25.1 µg of vitamin B_{12}/mg of protein. Molecular weights of 61,000 to 66,000 were obtained. The protein contains 35.5% carbohydrate. Hog nonintrinsic factor retains its monomeric form in the presence of vitamin B_{12} under conditions in which hog intrinsic factor aggregates. Hog intrinsic factor and hog nonintrinsic factor differ significantly from each other in their amino acid and carbohydrate composition. These differences, together with differences in other parameters, demonstrate that these 2 proteins are distinct and separate entities.

5600 THE EFFECT OF GLUCAGON ON SERUM GASTRIN. II. STUDIES IN PERNICIOUS ANAEMIA AND THE ZOLLINGER-ELLISON SYNDROME. *(E.)* Korman, M. G.; Soveny, C.; Hansky, J. (Prince Henry's Hosp., Melbourne, Australia). *Gut* 14(6):459-461, 1973.

To determine whether injection of glucagon, like injection of secretin, lowers the high serum gastrin levels in pernicious anemia and raises the gastrin level in Zollinger-Ellison syndrome, studies were performed in patients with the 2 diseases. Serum gastrin was measured by radioimmunoassay before and after injection of glucagon (1 mg, i.v.) in 4 patients (all females, aged 52-78 yr) with a pernicious anemia and 4 patients (2 males and 2 females, aged 37-62) with Zollinger-Ellison syndrome. The injection produced transient nausea in the pernicious anemia patients, this was not noted in the patients with Zollinger-Ellison syndrome. In each of the patients with pernicious anemia, glucagon caused a marked fall in serum gastrin; the maximum decrease occurred 15-20 min after injection, with a fairly rapid return to basal levels. In no case did the serum gastrin drop to the level reached when healthy subjects are injected with glucagon. In 3 of the patients with Zollinger-Ellison syndrome serum gastrin rose significantly on glucagon injection; the maximum rise occurred 10-45 min after injection. In the 4th patient, both the gastrin and acid outputs were measured and both rose almost simultaneously. The reason for the paradoxical rise in serum gastrin in response to glucagon in the Zollinger-Ellison syndrome is unknown. However, it is suggested that this rise be used in diagnosing the Zollinger-Ellison syndrome.

5601 THE EFFECT OF TEMPERATURE ON GEL FORMATION IN PIG-GASTRIC MUCUS. *(E.)* Snary, D.; Allen, A.; Pain, R. H. (Dept. Biochem. Univ. Newcastle-upon-Tyne, England). *Eur. J. Biochem.* 36(1):72-75, 1973.

The viscosity and gel properties of gastric mucus prepared from the superficial scrapings of the cardiac region of the pig stomach are due to a mucoprotein of protein content of 18% and molecular weight of 2 x 10^6. At 25 C, the reduced specific viscosity of this mucoprotein increases with increasing concentration until the mucoprotein undergoes a reversible sol-gel transition at concentrations above 4 mg/ml. For a given concentration of mucoprotein, the viscosity increases markedly with temperature, and at 45 C the threshold concentration for reversible gel formation is reduced to 2 mg/ml. The intrinsic viscosity corrected for zero shear, the shear dependence of the viscosity, and the sedimentation properties of the mucoprotein as a function of temperature have been measured. The increase of viscosity with temperature has been shown to be due to increased intermolecular interaction rather than structural changes in the molecule. The temperature dependence is characteristic of hydrophobic interactions, and the results suggest gel formation in gastric mucus takes place through the formation of micelle junctions involving hydrophobic interactions between soluble mucoprotein molecules.

5602 MAXIMAL ACID RESPONSE IN PAVLOV POUCH CATS TO PENTAGASTRIN AND FEEDING ALONE AND IN COMBINATION. *(E.)* Svensson, S.; Emas, S. (Allmanna Sjukhuset, Malmo, Sweden). *Gastroenterology* 5(1): 54-59, 1973.

In cats with both gastric fistulae and Pavlov pouches, the Pavlov pouch acid response to a single injection of 2-deoxy-D-glucose (100 mg/kg, i.v.) was unaltered by closing the gastric fistula. This suggests that the Pavlov pouch was vagally innervated and that duodenal acidification by closing the gastric fistula did not inhibit vagally stimulated Pavlov pouch secretion in cats. The maximum of the dose-response curve for Pavlov pouch acid output (gastric fistula closed) to graded doses of (0.5-64 μg/kg/hr, i.v.) and graded meat meals (3-50g, i.v.) was equal. Based on previous findings that the maximal response to feeding amounted to 70% of that to pentagastrin in cats with vagally denervated pouches, this study showed that vagal impulses to the Pavlov pouch during feeding increased the action of endogeneous gastrin released in amounts that alone produced submaximal response. Since concomitant maximal stimulation with pentagastrin did not increase the Pavlov pouch response to feeding, the increase of vagal tone by feeding did not potentiate the maximal response to pentagastrin. These results therefore suggest that the increased vagal tone to the Pavlov pouch evoked by feeding increased submaximal responses to gastrin but did not potentiate the maximal response. It is suggested that the cat might be a satisfactory model for studying the interaction of vagal impulses and gastrin on gastric acid secretion in man.

5603 EFFECT OF STIMULATORS AND INHIBITORS OF HYDROCHLORIC ACID SECRETION ON NUMBERS OF OXIDOREDUCTASE-POSITIVE GASTRIC PARIETAL CELLS IN RATS. *(E.)* Barbarino, F.; Fodor, O.; Popescu, S. (Inst. Public Health Med. Res., Cluj, Rumania). *Clin. Chim. Acta* 43(3):389-395, 1973.

Frequency counts of gastric parietal cells with positive reactions for 6 oxidoreductases (L-lactate, D-glucose-6-phosphate, succinate, reduced nicotinamide adenine dinucleotide, L-glutamate, and D-3-hydroxybutyrate) were performed in 30 rats treated with stimulators and inhibitors of hydrochloric acid secretion. Insulin (2 U) and reserpine (1.25 mg, i.p.) selectively increased the number of cells with positive histochemical reactions for enzymes involved in anaerobic glycolysis, the Krebs cycle, and the respiratory chain, and enhanced their predominance under basal conditions. Propantheline (0.6 mg, i.p.), secretin (4 U, i.p.), and depepsen (100 mg, in food), however, decrease the number of the same oxidoreductase-positive cells, thus reducing the differences between them and the enzymes belonging to other biochemical pathways (pentose phosphoric shunt, amino acid and ketone bodies metabolism). It seems probable that both stimulators and inhibitors selectively influence those enzymes whose activity offers a metabolic basis for hydrochloric acid secretion, which is the characteristic function of gastric parietal cells.

5604 EFFECT OF DEGLYCYRRHIZINIZED LIQUORICE ON GASTRIC ACID SECRETION, HISTIDINE DECARBOXYLASE ACTIVITY AND SERUM GASTRIN LEVEL IN THE RAT. *(E.)* Hakanson, R.; Liedberg, G.; Oscarson, J.; Rehfeld, J. F.; Stadil, F. (Dept. Pharmacol., Univ. Lund, Sweden). *Experentia* 29(5):570-571, 1973.

Acid secretion was studied in 8 male Wistar rats with chronic gastric fistulas. After basal acid secretion was collected for 2 1-hr periods, a deglycyrrhizinized liquorice preparation (200 mg/kg, i.p.) was given and 4 additional 1-hr portions collected. To determine histidine decarboxylase activity and gastrin in serum, 12 normal and 8 antrectomized rats were given the deglycyrrhizinized liquorice preparation (200 mg/kg, i.p., twice with a 3-hr interval). The i.p. injection of the preparation in a dose of 200 mg/kg caused a marked and highly significant reduction of the acid output in gastric fistula rats. The inhibition was apparent during the first hr and lasted for at least 4 hr. After 2 injections of the preparation, histidine decarboxylase activity in normal rats (5.2 pmoles CO_2/mg/hr) was increased to 18.4 pmoles CO_2/mg/hr; the activity in antrectomized rats did not increase (4.6 pmoles CO_2/mg/hr). Gastrin activity in normal rats (37 p Eq synthetic human gastrin/ml) was increased to 122 p Eq synthetic human gastrin/ml; gastrin activity is antrectomized rats did not increase (27 p Eq synthetic human gastrin/ml). It is likely that the inhibition of acid secretion contributes to the ulcer-protective action of the deglycyrrhizinized liquorice preparation. This inhibition is certainly not due to suppressed gastrin release or to inactivation of histidine decarboxylase. Perhaps the preparation exerts a direct effect on the parietal cell.

5605 GASTRIC SECRETORY RELATIONSHIP BETWEEN H^+ AND PEPSIN IN FISTULA CHICKENS. *(E.)*

Burhol, P. G. (Ulleval Hosp., Oslo, Norway). *Scand. J. Gastroenterol.* 8(3):283-288, 1973.

Pentagastrin (75, 150, 300, and 600 µg/kg/hr, s.c., for 120 min) was administered on separate days to each of 14 Plymouth Rock chickens with surgically implanted proventricular cannulas. Steady-state gastric secretion was achieved. Gastric H^+ and pepsin followed each other rather closely, as also indicated by closely similar secretory kinetics. Pentagastrin shifted the ratio of pepsin to H^+ secretion from one level to a higher one, and showed an unusually strong pepsigogue effect. It is concluded that the gastric H^+ and pepsin secretion is more closely related in birds than in mammals. The different effects of histamine and pentagastrin on pepsin secretion suggest that their gastric stimulatory effects are not mediated by a common mediator. It is also unlikely that histamine or gastrin-related substances can be the final mediator of the stimulus to initiate and sustain the gastric secretion.

5606 LIBERATION OF GASTRIN BY METHYLXANTHINE.

(Ger.) Miederer, S. E.; Kaess, H.; Stadelmann, O. (Med. Polyclin., Univ. Bonn, Germany). *Klin. Wochenschr.* 51(1):42-44, 1973.

A significant (65.1%) increase occurred in gastric acid concentrations, determined on 16 subjects after 45 min i.v. infusion of theophylline ethylenediamine (4.3 mg/min). However, a 3-min i.v. infusion of theophylline ethylenediamine (240 mg) had no effect on serum gastrin concentrations determined on 10 subjects by a radioimmunological method. Thus, it is unlikely that increases in gastric acid secretion induced by theophylline are caused by an increase in serum gastrin levels. These results, along with others in the literature, suggest that theophylline may act on parietal cells *via* a "second messenger" mechanism by blocking diphosphodiesterase.

5607 SENSORY DEPRIVATION ON VISCERAL ACTIVITY. IV. THE EFFECT OF TEMPORARY VISUAL DEPRIVATION ON CANINE GASTRIC SECRETION. *(E.)*

Schapiro, H.; Britt, L. G.; Dohrn, R. H. (Univ. Tennessee Med. Units, Memphis). *Am. J. Dig. Dis.* 18(7):573-575, 1973.

In 6 dogs, gastric cannulas were placed in the dependent part of the stomach. Of the 6, 3 also had esophagostomies. The total acid output/hr was determined after (1) teasing with meat, (2) sham-feeding with meat, (3) hypoglycemia and induced by insulin (1.0 U/kg, i.v.) and (4) the injection of histamine base (0.01 mg/kg, s.c.). The mean total acid output was established for each test condition for each dog. Temporary visual deprivation caused a mean 41% reduction in the total acid output after teasing with meat, a 73% depression after sham-feeding with meat, and a 18% reduction after histamine injection. No effect was observed after insulin-induced hypoglycemia. Since both the teasing with meat and sham-feeding stimuli arise in the central nervous system and are mediated via the vagus, it is suggested that temporary visual deprivation reduces central nervous system activity and/or gastric vagal activity.

5608 THE EFFECT OF AMINOPHYLLINE ON PENTAGASTRIN-INDUCED GASTRIC SECRETION IN THE DOG. *(E.)*

Gabrys, B. F.; Nyhus, L. M.; Van Meter, S. W.; Bombeck, C. T. (Abraham Lincoln Sch. Med., Chicago, Ill.). *Am. J. Dig. Dis.* 18(7):563-566, 1973.

The effect of aminophylline on gastric hydrochloric acid secretion was investigated in 5 dogs with a Heidenhain pouch or gastric fistula. Aminophylline (20 mg/kg, i.v.) administered during the resting state had no effect on gastric secretion. However, when this methylxanthine was administered during the secretory response to pentagastrin, (20 µg/kg/hr) it augmented the action of this peptide by 78% in dogs with Heidenhain pouches and by 53% in dogs with gastric fistula. On the basis of indirect evidence, it may be suggested that both agents act by increasing the cyclic AMP level in the gastric mucosa.

5609 INSULIN-STIMULATED GASTRIC ACID SECRETION AFTER VAGOTOMY IN MAN. *(E.)*

Cowley, D. J.; Baron, J. H. (Roy. Postgrad. Med. Sch., London, England). *Am. J. Dig. Dis.* 18(7):544-550, 1973.

The gastric acid response to insulin was studied in a group of patients with a history of chronic duodenal ulcer who had undergone incomplete truncal vagotomies and in 22 patients with complete vagotomies. A dose-response study of gastric acid secretion after insulin in 17 patients (16 men and 1 woman) with incomplete vagotomy indicated that a dose of 0.2 U/kg was greatly superior to 0.4 U/kg and marginally superior to 0.1 U/kg in eliciting the highest acid response.

Of the 17 patients with incomplete vagotomy, 8 "early" responders had a significantly greater peak acid output after insulin (0.2 U/kg), than 9 "late" responders, but only 1 early responder developed a recurrent ulcer compared with 4 patients in the late group. The timing of a patient's positive Hollander response to insulin was not related to the optimum dose of insulin in that patient. The blood glucose response to insulin (0.2 U/kg), was unchanged after complete vagotomy. The changes of blood glucose after a given dose of insulin varied from one individual to another. This variation could account for the finding that the dose which produced highest peak acid output in some individuals was 0.1 U/kg and in others, 0.2 U/kg. These results indicate that incomplete vagotomy does not alter the gastric secretory dose-response relation to graded doses of insulin in patients with a history of duodenal ulcer.

5610 THE EFFECT OF GLUCAGON ON SERUM GASTRIN. I. STUDIES IN NORMAL SUBJECTS. *(E.)* Hansky, J.; Soveny, C.; Korman, M. G. (Prince Henry's Hosp., Melbourne, Australia). *Gut* 14(6): 457-458, 1973.

The structural similarity of glucagon and secretin prompted an investigation into the effect of glucagon on basal serum gastrin in normal subjects. As determined by radioimmunoassay, glucagon (1 mg, i.v.), injected into 13 normal subjects (9 males and 4 females, aged 15 to 46 yr), caused basal serum gastrin levels to fall from 50.3 pg/ml to 9.4 pg/ml at 30 min after injection. Although the maximum fall occurred at 30 min, no significant difference between the levels at 15, 20, and 30 min was noted, indicating glucagon has a very rapid effect on serum gastrin. All subjects were affected. In 9 of the 13 subjects, serum gastrin fell to unmeasurable levels. The time of the fall suggests that the mechanism concerns interference with gastrin release but it is possible that there is a promotion of gastrin excretion.

5611 ANALYSIS OF INHIBITION OF ACID SECRETION IN ANESTHETIZED RATS. *(E.)* Schmidt, H. A.; Goebell, H.; Johannson, F. (Med. Clinic, Univ. Marburg, Germany). *Acta Hepatogastroenterol.* 20(1):51-57, 1973.

5612 EFFECT OF OXYPHENCYCLIMINE HCl ON BASAL GASTRIC SECRETION OF ACID AND PEPSIN IN MAN. *(E.)* Myren, J.; Berstad, A. (Ulleval Hosp., Oslo, Norway). *Acta Hepatograstroenterol.* 20(1):57-61, 1973.

5613 INFLUENCE OF FIXATION ON PHYSIOLOGICAL PROPERTIES OF FROG GASTRIC MUCOSA. *(E.)* Helander, H. F.; Rehm, W. S.; Sanders, S. S. (Med. Ctr., Univ. Alabama, Birmingham). *Acta Physiol. Scand.* 88(1):109-122, 1973.

5614 EFFECT OF A SULPHATED GLYCOPEPTIDE ON RAT GASTRIC ACID SECRETION STIMULATED BY HISTAMINE, BETHANECHOL, PENTAGASTRIN AND DIBUTYRYL CYCLIC AMP. *(E.)* Niada, R.; Prino, G. (Crinos Biol. Res. Lab., Villa Guardia, Italy). *Br. J. Pharmacol.* 48(3):550-552, 1973.

5615 A STUDY OF THE SELECTIVITY OF ACTION OF OXYPHENCYCLIMINE HYDROCHLORIDE ON GASTRIC SECRETION. (SELECTIVITY OF OXYPHENCYCLIMINE). *(E.)* Herrmann, R. P.; Sulway, M. J. (Roy. North Shore Hosp., Sydney, Australia). *Curr. Ther. Res.* 15(6):291-297, 1973.

5616 CALCIUM AND GASTROINTESTINAL SECRETION. *(E.)* Case, R. M. (Univ. Med. Sch., Newcastle upon Tyne, England). *Digestion* 8(3): 269-288, 1973.

5617 THE PENTOSE PHOSPHATE PATH FOR OXIDATIVE DEGRADATION OF GLUCOSE IN THE GASTRIC MUCOSA DURING HYDROCHLORIC ACID SECRETION. *(Rus.)* Epshtein, Ia. A. (I. P. Pavlov Inst. Physiol., Leningrad, USSR). *Dokl. Akad. Nauk SSSR* 211(5): 1233-1234, 1973.

5618 EFFECT OF THE SYMPATHETIC NERVOUS SYSTEM ON THE STOMACH METABOLIC PROCESSES. *(Rus.)* Zagorodneva, A. G.; Morgun, E. G.; Oleinik, I. F.; Svistun, T. I. (Bogomoletz Inst. Physiol. Acad. Sci. Ukr. SSR, Kiev, USSR). *Fiziol. Zh. SSSR* 59(6):940-944, 1973.

5619 PARTICIPATION OF THE SMALL INTESTINE IN THE TRANSMISSION OF INHIBITORY EFFECTS FROM THE SPHLANCHNIC NERVES TO THE GASTRIC GLANDS. *(Rus.)* Trefilov, A. B. (Med. Inst., Kursk, USSR). *Fiziol. Zh. SSSR* 59(7):1126-1129, 1973.

5620 ACTION OF PEPSIN ON SYNTHETIC SUBSTRATES. II. DIGLYCYL-L-PHENYLALANYL-L-PHENYLALANYL (AND L-TYROSYL)-GLYCINES: SENSITIVE SYNTHETIC SUBSTRATES FOR PEPSIN. *(E.)* Yonezawa, H.; Terada, S.; Izumiya, N. (Lab. Biochem., Fac. Sci., Kyushu Univ., Fukuoka, Japan). *J. Biochem. (Tokyo)* 73(4): 861-870, 1973.

5621 EFFECT OF SIMULATED MEAL SIZE ON GASTRIC ACID AND PEPSIN SECRETORY RATES IN BLUEGILL (LEPOMIS MACROCHIRUS). *(E.)* Norris, J. S.; Norris, D. O.; Windell, J. T. (Dept. Biol., Univ. Colorado, Boulder). *J. Fisheries Res. Bd. Canada* 30(2): 201-204, 1973.

5622 THE EFFECT OF DUODENAL REGURGITATION INTO THE CANINE STOMACH ON GASTRIC SECRETION. *(E.)* Wickbom, G.; Faith, M.; Woodward, E. R.; Dragstedt, L. R. (Univ. Florida Coll. Med., Gainesville). *J. Surg. Res.* 14(6):497-500, 1973.

5623 HOW RADIOIMMUNOASSAY HAS ADDED TO OUR KNOWLEDGE ABOUT GASTRIN. *(E.)* Grossman, M. I. (VA Wadsworth Hosp. Ctr., Los Angeles, Calif.). *Metabolism* 22(8):1033-1037, 1973.

5624 THE DEVELOPMENT AND APPLICATION OF ANTIBODIES TO GASTRIN. *(E.)* McGuigan, J. E. (Dept. Med., Univ. Florida, Gainesville). *Mt. Sinai J. Med. N.Y.* 40(3):365-373, 1973.

5625 NOREPINEPHRINE TURNOVER OF GLANDULAR STOMACH, DUODENUM AND HEART IN PENTAGASTRIN TREATED RATS. *(E.)* Djahanguiri, B.; Hemmati, M.; Abtahi, F. S. (Fac. Med., Univ. Tehran, Iran). *Res. Commun. Chem. Pathol. Pharmacol.* 6(1):357-360, 1973.

See also, 5626.

SECRETION AND METABOLISM

Pancreas

5626 THE EFFECT OF GLUCAGON ON THE FORMATION OF PANCREATIC JUICE AND BILE IN THE RAT. *(E.)* Shaw, H. M.; Heath, T. J. (Sch. Physiol. Pharmacol., Univ. New South Wales, Kensington, Australia). *Can. J. Physiol. Pharmacol.* 51(1):1-5, 1973.

The effect of porcine pancreatic glucagon on the formation of pancreatic juice and bile was studied in conscious male albino rats. When the rats were fasting, i.v. infusions of glucagon (7.2 μg/min/kg) were associated with depressions in the flow and in the output of bicarbonate and protein in pancreatic juice ($p < 0.001$). By contrast, infusions of glucagon to rats during feeding were associated with increases in the formation of pancreatic juice, particularly the volume and bicarbonate fraction. The responses were greater than those recorded in rats that did not receive exogenous glucagon during feeding ($p < 0.01$). Glucagon did not appear to influence the formation of bile.

5627 EFFECT OF GLUCAGON ON FOOD-INDUCED GASTROINTESTINAL SECRETIONS. *(E.)* Konturek, S. J.; Tasler, J.; Obtulowicz, W. (Med. Acad., Krakow, Poland). *Digestion* 8(3):220-226, 1973.

The action of glucagon on gastrointestinal secretion has been studied in 2 groups of 3 dogs each. In one group dogs were prepared with gastric fistulas, Pavlov pouches, and pancreatic fistulas, while dogs in the other group possessed only gastric and biliary fistulas. Glucagon (25 μg/kg/hr, i.v.) was infused during a steady state of half-maximal secretory response to food. Glucagon caused a maximal inhibition of gastric secretion to 60% of the control level. The effect lasted during infusion and persisted after withdrawal. Blood glucose increased during infusion, but fell when glucagon administration was stopped. Glucagon also caused an immediate reduction of pancreatic output. Bicarbonate output was inhibited to 75% and protein output to 45% of the control level. In 45 min after the withdrawal of glucagon, the protein and bicarbonate outputs had returned to normal levels. Glucagon had no effect on biliary secretion.

5628 PANCREATIC ACINAR CELLS: IONIC DEPENDENCE OF THE MEMBRANE POTENTIAL AND ACETYLCHOLINE-INDUCED DEPOLARIZATION. *(E.)* Matthews, E. K.; Petersen, O. H. (Dept. Pharmacology, Univ. Cambridge, England). *J. Physiol.* 231(2):283-295, 1973.

Intracellular recordings of membrane potentials have been made *in vitro* from the exocrine acinar cells of the mouse pancreas with glass micro-electrodes. The mean membrane potential of the acinar cells during superfusion with Krebs-Henseleit solution was - 39.2 mV. When $[K]_o$ was above 10 mM, increasing $[K]_o$ 10-fold decreased the membrane potential by 28 mV. This depolarization was not affected by atropine (1.4×10^{-6} M). Strophanthin G (10^{-3} M) slowly depolarized the cells at about 10 mV/hr. Brief exposure to acetylcholine (5.5×10^{-5} M) or pancreozymin resulted in a short lasting depolarization of the acinar cells. Atropine (1.4×10^{-6} M) blocked the depolarizing action of acetylcholine but not that of pancreozymin. Adrenaline ($5{\cdot}5 \times 10^{-5}$ M) or cyclic AMP (10^{-3}-10^{-4} M) did not influence the membrane potential. The amplitude of the acetylcholine-induced depolarization was not dependent on the presence of CO_2/HCO_3 in the bathing fluid, but it was closely dependent on the extracellular Na concentration. However, acetylcholine was still able to evoke a small depolarization even after prolonged exposure of the tissue to a Na-free solution. During exposure of the tissue to a Ca-free solution the resting membrane potential was decreased and the acetylcholine-induced depolarization was significantly reduced. Some substances which are known in other tissues to inhibit membrane Ca^{2+} currents, i.e. La^{3+}, D-600 and tetracaine, were able to reduce, but never abolish, the acetylcholine-induced depolarization. These results suggest that acetylcholine increases the permeability of the membrane of pancreatic acinar cells to commonly occurring ions with a consequent Na-influx and a small Ca-influx.

5629 IMMUNE REACTIONS TO FRACTIONS OF CRYSTALLINE INSULIN. I. SIGNIFICANCE OF LYMPHOCYTIC INFILTRATES IN THE ENDOCRINE AND EXOCRINE PANCREAS OF MICE. *(E.)* Freytag, G.; Jansen, F. K.; Kloppel, G. (Inst. Pathol., Univ. Hamburg, Germany). *Diabetologia* 9(3):185-109, 1973.

5630 DOES VAGAL STIMULATION LIBERATE SECRETIN AND/OR CHOLECYSTOKININ IN PIGS? *(E.)* Magee, D. F.; Sullivan, J. F. (Creighton Univ. Sch. Med., Omaha, Neb.). *Experientia* 29(5):565-566, 1973.

5631 A MODIFICATION OF TECHNIC FOR PANCREATODUODENAL TRANSPLANTATION IN DOGS. *(E.)* Seneca, R. P.; Dimler, M.; Cardenas, F. (Georgetown Univ. Med. Ctr., Washington, D.C.). *Am. Surg.* 39(4):244-249, 1973.

5632 MECHANISM OF ACTION OF PANCREOZYMIN AND ACETYLCHOLINE ON PANCREATIC ACINAR CELLS. *(E.)* Peterson, O. H. (Inst. Med. Physiol., Univ. Copenhagen, Denmark). *Nature* [*New Biol.*] 244(133): 73, 1973.

See also, 5586, 5712.

SECRETION AND METABOLISM

Hepatobiliary Tract

5633 THE EFFECT OF ETHANOL ON DRUG OXIDATIONS *IN VITRO* AND THE SIGNIFICANCE OF ETHANOL-CYTOCHROME P-450 INTERACTION. *(E.)* Cinti, D. L.; Grundin, R.; Orrenius, S. (Karolinska Inst., Stockholm, Sweden). *Biochem J.* 134(2):367-375, 1973.

The effect of ethanol on *N*-demethylation of aminopyrine in liver slices from male Sprague-Dawley rats and in the microsomal fraction and on microsomal hydroxylation of pentobarbital and aniline was studied. With liver slices *N*-demethylation of aminopyrine was stimulated by 35-40% at low ethanol concentrations (2mM). No stimulation occurred at high concentrations (100 mM); in fact, a 15-20% decrease in the rats of *N*-demethylation was often observed. With the liver microsomal fraction, no effect occurred with ethanol concentration up to 50 mM and an inhibitory effect was observed at high ethanol concentrations (100 mM). This was also observed with the other drugs studied. In agreement with these results, only at a high concentration did ethanol interfere with the binding of drug substrates to cytochrome *P*-450. Further, as previously reported, ethanol produced a reverse type I spectral change when added to the liver microsomal fraction. Evidence was found which indicated that this spectral change is due to removal of substrate, endogenously bound to cytochrome *P*-450. A dual effect of ethanol is assumed to explain the present findings; in liver slices, at a low ethanol concentration, the enhanced rate of drug oxidation is the result of an increased reduced nicotinamide adenine dinucleotide concentration, whereas the inhibitory effect observed with the microsomal fraction at high ethanol concentration is due to the interference by ethanol with the binding of drug substrates to cytochrome *P*-450.

5634 METABOLIC ALTERATIONS PRODUCED IN THE LIVER BY CHRONIC ETHANOL ADMINISTRATION. INCREASED OXIDATIVE CAPACITY. *(E.)* Videla, L.; Bernstein, J.; Israel, Y. (Dept. Pharmacol., Univ. Toronto, Canada). *Biochem. J.* 134(2):507-514, 1973.

Administration of ethanol (14 g/day/kg) for 21-26 days to male Wistar rats increases the ability of the animals to metabolize ethanol, without concomitant changes in the activities of liver alcohol dehydogenase or catalase. Liver slices from rats chronically treated with ethanol showed a 40-60% increase in the rate of oxygen consumption. The effect of uncoupling agents such as dinitrophenol and arsenate was completely lost after chronic ethanol treatment. Isolated mitochondria prepared from animals chronically treated with ethanol showed no changes in state 3 or state 4 respiration, ADP/O ratio, respiratory control ratio, or in the dinitrophenol effect when succinate was used as substrate. With β-hydroxybutyrate as substrate a small but statistically significant decrease was found in the ADP/O ratio but not in the other parameters or in the dinitrophenol effect. Further, no changes in mitochondrial Mg^{2+}-activated adenosine triphosphatase, dinitrophenol-activated adenosine triphosphatase, or in the dinitrophenol-activated adenosine triphosphatase/Mg^{2+}-activated adenosine triphosphatase ratio were found as a result of the chronic ethanol treatment. Liver microsomal reduced nicotinamide adenine dinucleotide phosphate oxidase activity was increased by 80-100% by chronic ethanol treatment. Oxidation of formate to carbon dioxide *in vivo* was also increased. The increase in formate metabolism could theoretically be accounted for by an increased production of hydrogen peroxide by the reduced nicotinamide adenine dinucleotide phosphate oxidase-system plus formate peroxidation by catalase. However, an increased production of hydrogen peroxide and oxidation of ethanol by the catalase system could not account for more than 10-20% of the increased ethanol metabolism in the animals chronically treated with ethanol. Results presented indicate that chronic ethanol ingestion results in a faster mitochondrial oxygen consumption *in situ* suggesting a faster reduced nicotinamide adenine dinucleotide reoxidation. Although only a minor change in mitochondrial coupling was observed with isolated mitochondria, the possibility of an uncoupling in the intact cell cannot be completely discarded. Regardless of the mechanism, these changes could lead to an increased metabolism of ethanol and of other endogenous substrates.

5635 EFFECTS OF ETHANOL AND FAT ON THE TRANSPORT OF REDUCING EQUIVALENTS INTO RAT LIVER MITOCHONDRIA. *(E.)* Cederbaum, A. I.; Lieber, C. S.; Toth, A.; Beattie, D. S.; Rubin, E. (Mt. Sinai Sch. Med., City Univ. New York, N.Y.). *J. Biol. Chem.* 248(14):4977-4986, 1973.

Chronic ethanol intoxication in male Sprague-Dawley rats accelerated the rate of ethanol metabolism 44-47%, but decreased the activity of alcohol dehydrogenase by 20%. Chronic consumption of ethanol decreased the activities of cytochrome oxidase and succinic dehydrogenase in liver mitochondria and in cell-free homogenates, whereas total hepatic mitochondrial protein was not altered by ethanol feeding. Thus, total "mitochondrial activity" was decreased and cannot account for the increased rate of blood ethanol clearance. Therefore, the activities of mitochondrial enzymes and those of "shuttle" systems for the transport of reducing equivalents into mitochondria were investigated. Reconstituted malate-aspartate, fatty acid, and α-glycerophosphate shuttles were equally effective in transporting reducing equivalents into the mitochondria from ethanol-fed and control rats. The activities of enzymes involved in the shuttles, such as cytoplasmic and mitochondrial α-glycerophosphate dehydrogenase and glutamic oxalacetic transaminase, were either decreased or unchanged by chronic ethanol consumption. The permeability of the mitochondria to reduced nicotinamide adenine dinucleotide and to substrate anions which participate in the shuttles was also not altered by ethanol feeding. It is therefore unlikely that the increased rates of ethanol oxidation produced by chronic ethanol consumption are caused by enhanced transport of reducing equivalents into the mitochondria. A high fat diet alone (35% of total calories) increased both the endogenous and total rates of shuttle activity, compared with the rates obtained with mitochondria from rats which had consumed a low fat diet. This suggests that, if the transport of reducing equivalents into the mitochondria is the rate-limiting step in ethanol metabolism, ethanol clearance rates *in vivo* should be higher in rats fed the high fat diet than in those fed low fat chow. However, the rates of blood ethanol clearance were comparable in rats consuming either diet. Thus, the transport of reducing equivalents into the mitochondria under these conditions is not rate-limiting for ethanol metabolism.

5636 SEPARATE POOLS FOR ENDOGENOUS AND EXOGENOUS CHOLESTEROL IN RAT INTESTINES. *(E.)* Sodhi, H. S.; Orchard, R. C.; Agnish, N. D.; Varughese, P. V.; Kudchodkar, B. J. (Dept. Med. Univ. Saskatchewan, Saskatoon, Canada). *Atherosclerosis* 17:197-210, 1973.

Endogenous and exogenous cholesterol were pulse labeled by injection of [2-^{3}H] mevalonate (10-20 μCi, i.p.) and by gastric intubation of [4-^{14}C]cholesterol (3-6 μCi) in male, Sprague-Dawley rats with common bile and thoracic lymph duct fistulae. After 3 hr some of the exogenous cholesterol appeared in the large intestines, although a significant fraction was still present in the stomachs of the rats. The specific activity of exogenous cholesterol reached peak values and then declined at rates much faster than those for endogenous cholesterol in thoracic duct lymph. The free/esterified specific activity ratios for the 2 isotopes were different in the lymph cholesterol but were similar for cholesterol in different segments along the intestinal tract. Cholesterol-fed rats (with cannulae in the common bile and thoracic lymph ducts) were given sustained intraduodenal infusions (20-24 hr) with normal rat bile to which [4-^{14}C]cholesterol and [2-^{3}H]mevalonate had been added. The specific activity for both isotopes in the lymph cholesterol increased rapidly and stabilized by 16 hr at values many times greater than the specific activity of liver, bile, or plasma cholesterol. On removal of radioisotopes from the infusate there was an exponential decline up to 30 hr in the specific activity of both isotopes. The rate of decline for ^{14}C was up to 3 times greater than that for ^{3}H. The specific activity ratios of free/esterified cholesterol in the lymph were also consistently different for 2 isotopes. These results suggest that dietary cholesterol absorption is considerably more efficient than the absorption of endogenous cholesterol synthesized in the intestines. These data also imply that the cholesterol derived from the two sources exists in different pools in the rat intestines.

5637 ROLE OF HEPATIC ANION-BINDING PROTEIN IN BROMSULPHTHALEIN CONJUGATION.

(E.) Kaplowitz, N.; Percy-Robb, I. W.; Javitt, N. B. (Cornell Univ. Med. Coll., New York, N.Y.). *J. Exp. Med.* 138(2):483-487, 1973.

By adding BSP to the supernatant from rat liver homogenate before Sephadex gel filtration, 3 protein fractions that bound BSP were isolated; one of these fractions was identified as Y protein or ligandin. When 2-^{3}H-glycine glutathione was added to BSP and soluble liver protein and the mixture was subjected to gel filtration, the elution volume of Y protein marked with BSP and that of glutathione were the same, indicating that Y protein binds both BSP and glutathione. Since the pattern of glutathione binding in the absence of BSP was the same, glutathione binding does not involve a glutathione-BSP conjugate. The same pattern of activity was found by assaying anion-binding protein fractions for glutathione S-aryltransferase activity when 2 different methods were used (^{35}S-BSP and glutathione or 3,4-dichloronitrobenzene and glutathione as cosubstrates). This indicates that a close relation, if not identity, exists between Y protein and S-glutathione aryltransferase. If Y protein acts both as an intracellular binding protein in the hepatic uptake of organic anions and as an enzyme that also metabolizes some of these anions, this would account for impairment of BSP clearance seen in liver disease or during biliary tract radiography.

5638 EFFECT OF PROTEIN DEFICIENCY ON THE INDUCIBILITY OF THE HEAPTIC MICROSOMAL DRUG-METABOLIZING ENZYME SYSTEM. II. EFFECT ON ENZYME KINETICS AND ELECTRON TRANSPORT SYSTEM.

(E.) Mgbodile, M. U.; Hayes, J. R.; Campbell, T. C. (Dept. Biochem. Nutr., Virginia Polytech. Inst. State Univ., Blacksburg). *Biochem. Pharmacol.* 22:1125-1132, 1973.

Male, weanling Sprague-Dawley rats divided into 3 groups were maintained for 15 days on a semipurified diet containing 5% casein fed *ad lib* (group 1), 20% casein pair-fed to group 1 (group 2), or 20% casein fed *ad lib* (group 3). After each group was further subdivided, animals were injected i.p. on days 11-14 with 0.9% saline or phenobarbital (80 mg/kg) in 0.9% saline. Animals were decapitated 24 hr after the final injection and liver microsomes were prepared. Apparent V_{max} and apparent K_m kinetic constants were determined for ethylmorphine and aniline. The V_{max}/mg of microsomal protein was 64-66% lower in the protein-deficient group. Equivalent reductions of the content of cytochrome P-450 and activities of cytochrome P-450 and *c* reductases were also observed. Phenobarbital induction increased specific enzyme activities (V_{max}/mg of microsomal protein) in all groups with slightly greater percentage increases seen in the protein-deficient animals. A 4.2- to 8.3-fold increase was noted for ethylmorphine. A 2.5- to 4.1-fold increase in specific enzyme activity was related to a 2.6- to 4.5-fold increase in P-450 content and a 6.0- to 7.9-fold increase in P-450 reductase activity. It is suggested that phosphatidylcholine and cytochrome P-450 play important roles in the kinetics of metabolism determined after protein deficiency or phenobarbital induction, or both.

5639 BILE ACIDS. XXXIX. METABOLISM OF 5α-CHOLESTANE-3β,26-DIOL AND 5α-CHOLESTANE-3β,7α,26-TRIOL IN THE RAT WITH A BILE FISTULA.

(E.) Noll, B. W.; Doisy, Jr., E. A.; Elliott, W. H. (St. Louis Univ. Sch. Med., Mo.). *J. Lipid Res.* 14(4):391-399, 1973.

The ketone, 3β,26-diacetoxy-5α[5α,6α-$^{3}H_2$]cholestan-7-one, was prepared from kryptogenin and used in turn to prepare 25R-5α-[5α,6α-$^{3}H_2$]cholestane-3β,7α,26-triol. Huang-Minlon reduction of the ketone provided 25R-5α-[5α-^{3}H]cholestane-3β,26-diol. Mass spectrometry, molecular rotation, and several types of chromatography give results consonant with assigned structures. Bile was collected for 8 days from adult male rats, with cannulated bile ducts, that had received approximately 0.8 mg of the triol or diol, i.p. Bile from the first 12 hr was hydrolyzed, and the bile acids were separated by partition chromatography. The chromatographic pattern of separated bile acids was much simpler for the triol than for the diol. Approximately 50% of the bile acids derived from the triol were trihydroxy allo acids (allocholic acid, 44%, and its 3β isomer, 5.3%); only 16.4% allocholic acid was obtained from the diol. Comparable amounts of allochenodeoxycholic acid were derived from the diol and triol (21.2% and 28.2%, resp.). Unidentified metabolites in the dihydroxy acid fraction derived from the diol constituted 15.8% of chromatographed material.

5640 ROLE OF ASCORBIC ACID IN CHOLESTEROL METABOLISM. FUNCTION OF VITAMIN C IN BILE ACID BIOSYNTHESIS.

(Rus.) Ginter, E. (Res. Inst. Nutr., Bratislava, Czechoslovakia). *Vopr. Pitan.* (1):29-35, 1973.

Studies performed on guinea pigs indicate that vitamin C takes part in the catabolism of cholesterol. A model of chronic latent vitamin C deficiency was developed in guinea pigs by giving them a vitamin C-deficient diet for 14 days and then administering a maintenance dose of vitamin C (0.5 mg/day). Chronic vitamin C deficiency significantly increased blood cholesterol levels and the cholesterol content of liver and skin; no decreases in cholesterol were found in any of the 12 tissues studied. When fed for 13-24 weeks to vitamin C-deficient guinea pigs, and atherogenic diet containing 0.3% cholesterol significantly increased the cholesterol content of the liver, adrenals, small intestine, and aorta. The extent of this increase in cholesterol depended upon the dose (0.5-50 mg/day) of vitamin C administered: the lowest cholesterol content were found in animals given the largest dose of vitamin C. When ^{14}C-labeled cholesterol was administered *via* a stomach tube to vitamin C-deficient guinea pigs, radioactivity in the gastrointestinal tract and feces was significantly higher than in controls while radioactivity in the blood and other organs was lower. Therefore, increased cholesterol levels in vitamin C-deficient guinea pigs cannot be accounted for by an increase in absorption of exogenous cholesterol since vitamin C deficiency inhibits cholesterol absorption. By administration of 4-^{14}C-cholesterol and 26-^{14}C-cholesterol to vitamin C-deficient guinea pigs, it was demonstrated that vitamin C deficiency decreased the conversion of cholesterol to bile acids in the liver and into exhaled CO_2. Administration of large doses of vitamin C (initial dose of 100 mg followed by 50 mg/day) to vitamin C-deficient guinea pigs significantly increased ^{14}C-cholesterol catabolism, as measured by increased expiration of $^{14}CO_2$. It is suggested that ascorbic acid takes part in the hydroxylation of cholesterol rings or its side chain.

5641 CAUSES OF ZONAL DISTRIBUTION OF GLYCOGEN IN THE LIVER ACINUS AFTER A FAT-RICH DIET.

(E.) Den Otter, W.; Blikkendaal-Lieftinck, L. F.; Koten, J. W. (Dept. Pathol., State Univ., Utrecht, Netherlands). *Experentia* 29(5):545-546, 1973.

In male Wistar WU rats on a 6-day fat-rich diet, RNA was mainly localized in zone 1 of Rappaport's liver acinus. Similar results were obtained for glycogen. Thus, a positive correlation exists between the localization of glycogen and RNA after a fat-rich diet. Controls, fed a carbohydrate-rich diet, showed glycogen and RNA spread out over the whole liver acinus. On a 50-day diet, glycogen and RNA disappeared completely from zone 3. Fatty acids determined after a 6-day fat-rich diet amounted to 12% of the wet weight of the liver. After 24 hr starvation the fatty acid content decreased 3%, but this lipid loss was not accompanied by glycogen synthesis in zone 3. In rats fed a carbohydrate-rich diet, followed by a 2 day starvation period, about 3% glycogen was synthesized within 4 hr. This was deposited mainly in zone 1 after a 6-day initial diet, but solely in zone 1 after a 50-day diet. These results imply that the RNA-rich cells in zone 1 are young and the more RNA-deficient cells in zone 3 are old. The loss of RNA in zone 3 is aggravated by lipids since the older cells have less resistance to lipid than the younger cells of zone 1. The presence of glycogen in zone 1 after a fat-rich diet indicates that recently regenerated liver cells receive a normal enzyme content. As they become older and move to the vena centralis, the enzyme content changes as influenced by age and diet.

5642 INTERRELATIONSHIP OF BILE SALTS, PHOSPHOLIPIDS, AND CHOLESTEROL IN BILE DURING MANIPULATION OF THE ENTEROPHEPATIC CIRCULATION IN THE CONSCIOUS DOG.

(E.) Soloway, R. D.; Powell, K. M.; Senior, J. R.; Brooks, F. P. (Univ. Pennsylvania Sch. Med., Philadelphia). *Gastroenterology* 64(6):1156-1162, 1973.

The interrelations of the biliary concentrations of bile salts, phospholipids, and cholesterol in the conscious dog were evaluated during complete interruption of the enterohepatic circulation, partial replacement of the enterohepatic circulation with i.v. taurocholate or infusions of secretin. Enterohepatic circulation interruption in the dog caused a fall in the concentrations and outputs of all three components; cholesterol concentration decreased relatively less than that of bile salts and phospholipids, but in contrast to man, enouch of the latter components remained to keep cholesterol solubilized in micelles. Taurocholate increased bile salt, cholesterol, and phospholipid outputs. After cessation of the secretin infusion during interruption, bile salt concentrations were unchanged; outputs of all 3 components were lower than controls. However, no change in the outputs of these components occurred when secretin was infused together with taurocholate. Regression equations, relating bile salt output to cholesterol and phospholipid output, indicated that during enterohepatic circulation interruption a portion of biliary cholesterol, but not phospholipids, is secreted independently of bile salts. The lack of formation of lithogenic bile with enterohepatic circulation interruption, together with the normally low biliary concentration of cholesterol, may account for the rarity of gallstone formation in the dog. In the absence of returning bile salts from extrahepatic sites, secretin impaired the synthesis and/or the secretin of bile salts, thus supporting recent findings that secretin is active at sites other than those concerned with the secretion of water and electrolytes.

5643 THE INTERRELATIONSHIP BETWEEN FRUCTOSE AND ETHANOL METABOLISM IN THE ISOLATED PERFUSED PIG LIVER.

(E.) Damgaard, S. E.; Sestoft, L.; Lundquist, F.; Tystrup, N. (Dept. Biochem. A, Univ. Copenhagen, Denmark). *Acta Med. Scand. (Suppl.)* 542:131-140, 1973.

The rate of ethanol elimination is about 0.7 µmol/min/g in the isolated perfused pig liver. The acetate produced from ethanol is metabolized at a rate of about 0.5 µmol/min/g. Metabolism of ethanol does not affect oxygen or acetate uptake in this preparation. Alcohol dehydrogenase activity in pig liver is about 2 µmol/min/g and is assumed to account for practically all of the ethanol oxidation observed under the experimental conditions. Fructose increases the ethanol elimination rate to more than twice the control value. Oxygen consumption is similarly increased during this stimulation. A relation between the fructose elimination rate and the stimulation of ethanol elimination is obtained. Pyruvate (concentration in the medium reaching 1.3 and 20 mmoles/liter) and D-glyceraldehyde (2 and 4 mmoles/liter) stimulate ethanol elimination, but in both cases the increase is less than 50% of the increase observed with fructose. Uncoupling of oxidative phosphorylation from respiration by dinitrophenol does not affect the basal ethanol elimination rate, but does decrease the fructose effect on ethanol oxidation to less than half. Accumulation of reduced metabolites during stimulation of ethanol elimination by fructose and D-glyceraldehyde only accounts for a minor part of this effect. It is assumed, therefore, that an energy dependent cyclic process (the 'malic enzyme shuttle') converts the reduction equivalents produced in the alcohol dehydrogenase reaction as reduced nicotinamide adenine dinucleotide to reduced nicotinamide adenine dinucleotide phosphate.

5644 EXPERIMENTAL HYPERBILIRUBINEMIA: EFFECT ON GLOMERULAR FILTRATION.

(E.) Aylward, T. D.; Schowengerdt, C. G.; Bove, K. (Cincinnati VA Hosp., Ohio). *J. Surg. Res.* 15(1)1-3, 1973.

To determine if there is a deterioration of renal function associated with chronic high levels of serum bilirubin, creatinine clearances were followed in dogs prepared with a "hyperbilirubinemia shunt". This shunt was constructed in 12 animals by dividing the common bile duct, ligating the distal end of the duct, and inserting one end of a polyethylene catheter into the proximal duct lumen, with the other end in the inferior vena cava via a left suprarenal vein. Six of the 12 animals also underwent cholecystectomy at the same time. Of the 12 shunted dogs, 11 showed an average decrease in the creatinine clearance rate of 54%. Decrease in clearance related directly to degree of bilirubinemia. At autopsy 3 animals showed mild cholangitis, and central necrosis occurred in 4. The most common renal alteration was the deposition of a granular bile pigment within the cytoplasm of intact convoluted tubular epithelial cells. Plasma volume in shunted animals was 21% lower than that of controls. It was suggested that, in the absence of prominent glomerular alterations, a reduced circulating blood volume may result in a decreased perfusion of glomeruli and a reduced glomerular filtration rate as rejected by decreased creatinine clearance; or, that intrarenal shunts may produce a blood flow that does not perfuse glomeruli and thus produce a reduced glomerular filtration rate.

5645 ROLE OF MICROTUBULES IN LIPOPROTEIN SECRETION BY THE LIVER.

(E.) Orci, L.; Le Marchand, Y.; Singh, A.; Assimacopoulous-Jeannet, F.; Rouiller, C.; Neanrenaud, B. (Inst. Histol. Embryol., Geneva, Switzerland). *Nature (Lond.)* 244(5410):30-32, 1973.

In mouse livers perfused for 2 hr in the presence of mitotic-spindle inhibitors, a marked decrease in the release of triglyceride-rich lipoprotein particles was noted. Vincristine (2.5 x 10^{-6}M) decreased triglyceride output from 17.7 to 5.9 µmol/100 g. Neither the uptake of oleate nor fatty acid oxidation to ketone bodies was affected, suggesting the absence of any related change in fatty acid metabolism. No modifications of any glucose production, ureogenesis, oxygen consumption, or cellular ATP content occurred. Labeled oleate incorporation into liver triglycerides was increased, indicating that triglyceride accumulation was occurring, even though it was not chemically detectable. The only observed ultrastructural changes appeared to be an accumulation of vacuoles containing very low density lipid-like particles, together with a disorganization of the microtubular system. From these observations it is suggested that colchicine and vincristine produce specific effects on microtubular structure and function, interfering with the orderly movement of triglyceride-rich lipoprotein particles to the extracellular space. It is proposed that the integrity of the microtubular system is required for the intracellular translocation of triglyceride-rich lipoprotein particles, and therefore, this system is essential in the sequence of events leading to lipoprotein secretion by the liver.

5646 THE EFFECT OF FRUCTOSE ON HEPATIC SYNTHESIS OF FATTY ACIDS.

(E.) Zakim, D. (San Francisco VA Hosp., Calif.). *Acta Med. Scand.* (suppl. 542):205-214, 1972.

The synthesis of fatty acids from fructose and glucose in rat and human liver is compared in an *in vitro* system using tissue slices. In both species fructose is a better percursor of fatty acids than glucose, primarily as a result of the greater rate of glycolysis of fructose. The high rate of fructose utilization and relatively low rates of glucose utilization by liver is reflected by the activity of fructokinase which is considerably greater than the total hexokinase and glucokinase activities. Although the high rate of fructolysis does produce a metabolic intermediate which alters the functional state of the fatty acid synthesizing enzymes, experimental evidence indicates that hepatic fatty acid synthesis in carbohydrate-fed animals is limited by the supply of substrate. Because the hepatic metabolism of fructose can supply acetyl-coenzyme A to the fatty acid synthesizing enzymes at greater rates than can the hepatic metabolism of glucose, hepatic fatty acid synthesis is enhanced in fructose- or sucrose-fed animals. Since estimates of maximum rates of fatty acid synthesis in human liver based on *in vitro* measurement of the activity of acetyl-coenzyme A carboxylase suggest that *de novo* synthesis of fatty acids in human liver can be large in comparison to the turnover of triglycerides in very low density lipoproteins, the data are compatible with the conclusion that enhanced rates of hepatic fatty acid synthesis contribute significantly to fructose- or sucrose-induced hypertriglyceridemia in normal men.

5647 NEUROHUMORAL CONTROL OF BILE SECRETION IN THE CHOLECYSTECTOMIZED, CONSCIOUS DOG.

(E.) Pissidis, A. G.; Nyhus, L. M.; Bombeck, C. T. (Abraham Lincoln Sch. Med., Univ. Illinois, Chicago). *Surgery* 74(1):122-129, 1973.

To clarify the interaction of neural and hormonal mechanisms in the regulation of bile secretion, the gallbladder was excised in 7 healthy mongrel dogs, a Thomas cannula placed in the duodenum opposite the papilla of the common bile duct, and 3 types of manipulations performed: hormonal stimulation with pentagastrin (2 µg/kg/hr, i.v.) or secretin (2 U/kg/

r); vagal stimulation with 2-deoxy-d-glucose (100 mg/
g, i.v.) and duodenal neutralization by continuous
rrigation of the duodenum below the pylorus with
.1N NaOH. In animals without duodenal neutraliza-
ion, each agent produced a marked stimulation of
ile volume during the hour immediately following
dministration, ranging from a 62% increase for
entagastrin and secretin stimulation to a 75%
ncrease for 2-deoxy-d-glucose. All agents produced
more dilute bile than observed during the basal
eriod, slightly increased bicarbonate concentration
nd total bicarbonate output, and a fall in tauro-
holate concentration. Under conditions of a neutra-
ized duodenum, however, the effect of pentagastrin
n bile volume and bicarbonate output was abolished,
hile the corresponding effects of 2-deoxy-d-glucose
nd secretin continued. With regard to effect on
aurocholate concentration under the conditions of
neutralized duodenum, secretin continued to produce
fall, while pentagastrin had a lesser effect and
-deoxy-d-glucose had the least effect. It is
uggested that alkalinization of the duodenum may
revent secretin release by any other stimulus, e.g.,
y pentagastrin.

648 METABOLISM OF FRUCTOSE AND GLYCERALDEHYDE IN THE ISOLATED PERFUSED PIG LIVER. *(E.)*

estoft, L.; Damgaard, S.; Tygstrup, N.; Lundquist,
. (Dept. Biochem., Univ. Copenhagen, Denmark). *Acta*
ed. Scand. (suppl. 542):119-129, 1972.

ructose uptake and the production of a number of
etabolites were measured in relation to the fructose
oncentration in the perfusion medium used to perfuse
solated pig livers under almost physiological con-
itions. A Michaelis type kinetics was found with V_m
out 3 μmol/g liver/min and K_m about 5 mM. Fructose-
-phosphate accumulated as a result of the inhibition
f the aldolase step, presumably by glyceraldehyde,
MP and inosine monophosphate. Under these experi-
ental conditions sorbitol formation is of small im-
ortance. The concentration of glyceraldehyde was
ess than 0.5 mM during continuous fructose infusion.
herefore, the metabolism of glyceraldehyde was stud-
ed separately. Measurement of the reaction products,
lycerol and glycerate, as a function of the glycer-
ldehyde concentration supports the hypothesis that
lyceraldehyde is metabolized by several pathways.
easurement of acid production during metabolism of
ither fructose of D-glyceraldehyde suggests that a
onsiderable accumulation of acids occurs in the
iver, as only a minor part of the titration value is
ccounted for through formation of lactose and glu-
ose. The rest was oxidized or accumulated in some
orm in the liver. During fructose metabolism oxygen
onsumption was increased about 30%, and the lactate/
yruvate ratio underwent small, but reproducible
hanges.

49 SHARED AND SEPARATE PATHWAYS FOR BILIARY EXCRETION OF BILIRUBIN AND BSP IN RATS.

E.) Clarenburg, R.; Kao, C. C. (Coll. Vet. Med., Kansas State Univ., Manhattan). *Am. J. Physiol.* 225(1):192-200, 1973.

The influence of bilirubin on biliary excretion of BSP was studied to determine whether multiple excretory processes exist for various anions, and to interpret BSP clearance tests in the presence of hyperbilirubinemia. Bilirubin was infused into male Charles River rats at the lowest rate establishing its maximal biliary excretion. When increasing amounts of BSP were infused simultaneously with that dose of bilirubin, increasing amounts of BSP were excreted, with only slightly decreasing the excretion maximum for bilirubin, until a combined excretion maximum for a BSP plus bilirubin was reached at 1:1 M ratio of infused anions. Elevating BSP dosage rates above that level resulted in mole-to-mole competition with bilirubin for biliary excretion. The results are explained by this model: low BSP dosages compete with bilirubin for excretion *via* a primary process; intermediate BSP dosages are chiefly excreted *via* a second process, not open to bilirubin; and high BSP dosages, saturating the second process, are excreted *via* the primary process in mol-to-mol competition with bilirubin. Capacities and K_m values of bilirubin and BSP excretion by the two processes are defined.

5650 INTESTINAL BILE ACIDS AND CHOLESTEROL ABSORPTION IN THE GERMFREE RAT. *(E.)*

Wostmann, B. S. (Dept. Microbiol., Univ. Notre Dame, Indiana). *J. Nutr.* 103(7):982-990, 1973.

Since germfree rats fed moderate amounts of cholesterol with their diet had 2 to 3 times higher liver cholesterol contents than comparable conventional rats and since there are profound differences between bile acid patterns in the feces of germfree and conventional rats, the present study was carried out to determine whether a change in the bile acid pattern of the bile itself in germfree animals would enhance the dietary uptake of cholesterol. It was found that the bile of adult male Wistar germfree rats fed diets low in cholesterol (0.05% or less) contained approximately 3 times as much bile acids as found in conventional rat bile. The taurocholic acid content was 1.6 to 1.7 times and higher and the tauro-β-muricholic acid approximately 10 times higher in bile from germfree than from conventional rats. In germfree bile taurocholic acid and tauro-β-muricholic were present in about equal amounts, and together accounted for 98% of the total bile acids. The biliary bile acid composition of the germfree rat was quite similar to the pattern found in its feces, except for a moderate preponderance of tauro-β-muricholic acid in the feces resulting from preferential reabsorption of taurocholic acid in the ileum of the germfree rat. Bile acid composition and concentration in the small intestine reflect the hepatic input. Throughout the small intestine bile acid concentrations of germfree rats were approximately 3 times higher than in conventional rats. The germfree rats absorbed 25% more labeled dietary cholesterol. The cholesterol accumulation found in the germfree rat fed cholesterol-containing diets may, therefore, be caused not only by reduced elimination *via* bile acids, but also, indirectly, by enhancement of the absorption of dietary lipids.

5651 FRUCTOSE AND LIVER PROTEIN SYNTHESIS. *(E.)* Maenpaa, P. H. (Dept. Med. Chem., Univ. Helsinki, Finland). *Acta Med. Scand.* (suppl. 542): 115-118, 1972.

D-fructose (5 mM/kg, i.v.) administered to rats inhibited by more than 90% incorporation of ^{14}C-leucine into liver protein. The inhibition was maximal 2 to 5 min after fructose injection and was practically over 25 min later. Inhibition of ^{14}C-leucine incorporation was closely correlated with the depletion of ATP. It is suggested that fructose inhibits amino acid incorporation by blocking aminoacylation. Liver polysome profiles were essentially unaltered 5 min after administration of fructose, but at 15 and 30 min a gradual and extensive disaggregation of large polysomes into monosomes was observed, indicating that the ribosomes are incapable of initiating a new cycle of peptide synthesis. Changes in the hepatic levels of free magnesium are thought to be involved in alterations of the polysome profiles after fructose administration.

5652 ACCUMULATION OF AMINO ACIDS BY THE PERFUSED RAT LIVER IN THE PRESENCE OF ETHANOL. *(E.)* Krebs, H. A.; Hems, R.; Lund, P. (Radcliffe Infirm., Oxford, England). *Biochem. J.* 124(3):697-705, 1973.

The presence of other metabolizable substances, especially fatty acids, ornithine and ethanol affects the rate of gluconeogenesis from alanine in the perfused liver from female Wistar rats. Gluconeogenesis is accelerated by oleate and by ornithine. When both oleate and ornithine were present, the acceleration was greater than expected on the basis of mere additive effects. Much ammonia and some urea were formed from alanine when no ornithine was added. With ornithine almost all the nitrogen released from alanine appeared as urea. Lactate was a major product of alanine metabolism. Lactate formation was decreased by addition of oleate, especially of oleate plus ornithine. Ethanol had no major effect on gluconeogenesis from alanine when this was the sole added precursor. Gluconeogenesis was inhibited by 87% when oleate was also added. However, ethanol greatly accelerated gluconeogenesis when ornithine was added together with alanine. In the absence of ethanol the alanine carbon and alanine nitrogen were recovered as glucose, lactate, pyruvate, ammonia and urea. In the presence of ethanol the balance of both alanine carbon and alanine nitrogen showed substantial deficits, largely accounted for by the formation of aspartate and glutamine, which was increased 2- to 3-fold. When alanine was replaced by lactate plus ammonium chloride, ethanol also caused a major accumulation of amino acids, especially of aspartate and alanine. Earlier, apparently conflicting results on the effects of ethanol on gluconeogenesis from alanine can be accounted for since, under well defined conditions, ethanol can inhibit, accelerate, or be without major effect on the rate of gluconeogenesis. In the synthesis of urea through the ornithine cycle, half of the nitrogen must be supplied in the form of aspartate and half in the form of carbamoyl phosphate. The accumulation of aspartate and other amino acids suggests that ethanol interferes with the control mechanisms which regulate the stoichiometric formation of aspartate and carbamoyl phosphate.

5653 MODIFICATION OF METABOLIC EFFECTS OF ETHANOL BY FRUCTOSE. *(E.)* Ylikahri, R. H.; Kahonen, M. T.; Hassinen, I. (Dept. Med. Chem., Univ. Helsinki, Finland). *Acta Med. Scand.* (suppl. 542):141-150, 1972.

To determine effects of fructose on ethanol-induced changes in carbohydrate metabolism and on acute ethanol-induced fatty liver, measurements of blood ethanol, fructose, glucose, triglycerides, and fatty acids and of liver triglycerides were made in rats fed 8.7 g/kg glucose, 8.7 g/kg fructose, 5.0 g/kg ethanol, 8.7 g/kg glucose + 5.0 g/kg ethanol, or 8.7 g/kg fructose + 5.0 g/kg ethanol. Blood ethanol concentrations were significantly higher in animals receiving only ethanol, due to accelerated ethanol elimination by fructose and glucose. Blood fructose concentrations were always low, due to slow absorption of fructose and to rapid uptake by the liver. When glucose was combined with ethanol, the blood glucose absorption was increased, due to glycogenolysis caused by ethanol in the liver. Fructose alone increased the blood glucose concentration. Ethanol augmented this effect, indicating that fructose is rapidly converted to glucose, even during ethanol metabolism. Thus it is concluded that although ethanol may inhibit the production of glucose from fructose *in vitro*, fructose rapidly abolishes the hypoglycemia induced by ethanol *in vivo*. A significant rise in the hepatic α-glycerophosphate concentration was noted 4 hr after ethanol feeding. Both glucose and fructose augmented this effect. The dihydroxyacetone phosphate concentration remained almost unchanged; thus, during acute intoxication, both fructose and glucose augment the redox effect of ethanol. Both fructose and glucose increased the hepatic triglyceride content, but the effect of ethanol was significantly greater. In all groups receiving ethanol, the changes in serum triglyceride concentrations were about the same. Serum free fatty acid was increased by ethanol, but decreased by ethanol combined with either glucose or fructose. The results show that altough the reduction of the hepatic redox state is one of the essential changes underlying the production of fatty acid by ethanol, it is not the only important factor. Inhibition of peripheral lipolysis is one factor involved in the inhibitory action of fructose and glucose on ethanol induction of fatty liver, but probably not the only one.

5654 BILIARY EXCRETION OF BILE ACIDS, LECITHIN, AND CHOLESTEROL IN HAMSTERS WITH GALLSTONES.

(E.) Wheeler, H. O. (Dept. Med., Univ. California, San Diego) *Gastroenterology* 65(1):92-103, 1973.

Young hamsters fed a lithogenic diet, deficient in essential fatty acid, showed an incidence of gallstones of 68%. When the diet was supplemented with 2% ethyl linoleate, the incidence dropped to 40%; 0.1% hyodeoxycholic acid reduced the incidence to zero. Control hamsters fed Purina lab chow showed no gallstones. Hepatic bile concentrations of cholesterol rose from 3.6 mol% for the controls to 8.8 mol% for the lithogenic group; the ratio of cholesterol to lecithin rose from 0.280 to 0.573; the ratio of lecithin to bile acid, from 0.164 to 0.216. The hyodeoxycholic acid caused a rise in cholesterol from the value of 3.6 mol% for the controls to the extremely high value of 25.8 mol% and a rise in lecithin from the value of 13.5 mol% for the controls to 21.3 mol%. During infusion of sodium glycocholate (at both 0.02 and 0.2 µmole pr min i.v.) the lithogenic group had relatively high lecithin to bile acid ratios but the highest ratios occurred after hyodeoxycholic acid. Cholesterol output in response to bile acid secretion was also increased in the lithogenic group and markedly increased after hyodeoxycholic acid. The lithogenic diet appeared to: (1) increase the availability of cholesterol, and amount of lecithin carried into the bile by bile acid secretion. Hyodeoxycholic acid caused extremely high biliary lipid output (possibly by a toxic effect on membranes), and thus may prevent solid gallstone formation by causing cholesterol to be excreted as a liquid crystal or gel.

5655 METABOLIC ALTERATIONS PRODUCED IN THE LIVER BY CHRONIC ETHANOL ADMINISTRATION. COMPARISON BETWEEN THE EFFECTS PRODUCED BY ETHANOL AND BY THYROID HORMONES. *(E.)* Israel, Y.; Videla, L.; Macdonald, A.; Bernstein, J. (Dept. Pharmacol., Univ. Toronto, Canada). *Biochem. J.* 134(2):523-529, 1973.

Liver slices from adult male Wistar rats treated with thyroxine (6 mg/kg i.p.) showed a 36% increased rate of oxygen consumption. The extra consumption, but not the basal respiration, is abolished by ouabain. Dinitrophenol caused a 50% increase in oxygen consumption by livers in control animals; it was not effective in increasing the rate of O_2 consumption of liver slices from thyroxine-treated animals but its effectiveness could be recovered in the presence of ouabain. (Na^+ + K^+)-stimulated adenosine triphosphatase activity of liver was increased 70% by administration of thyroxine *in vivo*. No changes were found in total Mg^{2+}-stimulated adenosine triphosphatase activity. Mitochondrial α-glycerophosphate dehydrogenase was increased 180% by thyroxine and 190% by chronic ethanol treatment. Both treatments also increased microsomal NADPH oxidase activity. In liver slices from animals chronically treated with ethanol urea synthesis increased from 12.7 to 19.3 µmol/hr/g. Mitochondrial size (sectional area) is markedly increased in the liver of animals chronically treated with ethanol. Acute administration of ethanol in doses of 4 and 6 g/kg increased the uptake, of ^{131}I-labelled thyroxine by the liver 30% and 55%, resp. Marked similarities are thus indicated between the effects produced in the liver by chronic administration of ethanol and by thyroid hormones.

5656 NATURALLY OCCURRING CHOLELITHIASIS IN A RHESUS MONKEY AND ITS EFFECT ON PLASMA AND AND BILIARY LIPID CONCENTRATIONS. *(E.)* Martin, D. E.; Wolf, R. C.; Houser, W. D. (Sch. Allied Health Sci., Georgia State Univ., Atlanta). *Am. J. Vet. Res.* 34(7):971-974, 1973.

Naturally occurring cholelithiasis was observed in an otherwise apparently normal female rhesus monkey. Samples of peripheral blood and gallbladder bile were obtained before, during, and after pregnancy to determine cholesterol, phospholipids, and total lipids; biliary bile salt concentrations were estimated. At necropsy several months later, pathologic changes were seen only in the edematous walls of the gallbladder which contained stones. Biliary cholesterol concentration was more than twice the normal value, without evidence of increased plasma cholesterol concentration. Biliary phospholipids and bile salts, as well as plasma phospholipids, generally were at concentrations observed in normal rhesus monkeys. Apparently, the unusually high biliary cholesterol content alone, unaccompanied by any significant decrease in biliary phospholipids or bile salts, was responsible for the precipitation. The cause of the increased biliary cholesterol was not determined.

5657 MALIGNANT TUMOURS OF LIVER AND LUNG IN RATS FED AMINOPYRINE OR HEPTAMETHYLENEIMINE TOGETHER WITH NITRITE. *(E.)* Lijinsky, W.; Taylor, H. W.; Snyder, C.; Nettesheim, P. (Biol. Div., Oak Ridge Natl. Lab., Tenn.) *Nature* 244(5412):176-178, 1973.

Groups of 15 male and 15 female Sprague-Dawley rats were given drinking water solutions containing heptamethyleneimine hydrochloride, 2 g/liter + sodium nitrite, 2 g/liter; aminopyrine, 1 g/liter + sodium nitrite, 1 g/liter; or aminopyrine, 250 mg/liter + sodium nitrite, 250 mg/liter. Of the control animals, which were fed nitrite, aminopyrine, or heptamethyleneimine alone, 1 died accidentally and 1 died from a large mammary tumor. Of those 30 animals fed 1 g/liter aminopyrine + nitrite, all died within 1 year, 29 with hemangioendothelial sarcomas of the liver which were highly malignant, metastases of the lung occurring in 17 animals. Of the 30 animals receiving the lower dose of aminopyrine + nitrite, 14 died in the first year, 12 with liver tumors, 1 with parotid tumor, and 1 with a large mammary tumor. Metastases of the lung occurred in 6 animals with tumors. In the 30 animals fed heptamethyleneimine + nitrite, 23 died in the first year, 20 developing primary tumors in 1 or more sites including papillomas (17 animals), squamous cell carcinoma of the lung (13), nasal turbinates, pharynx, tongue, and trachea. Squamous cell carcinomas metastasized to the kidney in 2 animals. The results suggest that the interaction of secondary and tertiary amines with nitrite in the stomach may represent an important facet of the etiology of cancer in man. The doses used here do not greatly exceed those encountered in human experience, yet a high tumor incidence was observed after 28-50 weeks of treatment, as a result of nitrosamine formation.

5658 COLLAGEN SYNTHESIS BY MESENCHYMAL CELLS ISOLATED FROM NORMAL AND ACUTELY-DAMAGED MOUSE LIVER.

(E.) Shaba, J. K.; Patrick, R. S.; McGee, J. O'D. (Roy. Infirm., Glasgow, Scotland). *Br. J. Exp. Pathol.* 54:110-116, 1973.

Mesenchymal cells were isolated from normal liver of Swiss albino mice and from liver acutely damaged by a single dose of carbon tetrachloride administered by esophageal tube. The majority of viable mesenchymal cells had the ultrastructural features of marcophages, while the remainder probably included perisinusoidal cells. Mesenchymal cells isolated from mice with acute liver damage had twice as much collagen synthetic activity as cells from normal liver. Mesenchymal cells from normal mouse liver also possessed collagen proline hydroxylase activity in addition to their ability to form the substrate for this enzyme. It is possible that the cell separation procedure (pronase digestion) stimulated transformation of liver sinusoidal lining cells to typical Kupffer cells. While macrophages in healing wounds and blood monocytes are known to transform to collagen-producing fibroblasts, it is unlikely that this function would precede a morphological change in cell type. However, the physical appearance of cells with the morphology of macrophages appears to have some role in fibrogenesis.

5659 ANIMAL MODEL: AFLATOXIN CARCINOGENESIS IN THE RAT.

(E.) Newberne, P. M.; Rogers, A. E. (Dept. Nutrition Food Sci., Massachusetts Inst. Technol., Cambridge). *Am. J. Pathol.* 72(1):137-140, 1973.

Weanling Charles River CD, Fischer, and Wistar rats fed low dietary concentrations of aflatoxin B_1 (0.1-1.0 ppm) develop liver cell carcinoma after 12-18 months. The same result is obtained by giving aflatoxin B_1 in 15 daily intragastric doses of 25 μg each in 0.1 ml dimethylsulfoxide. Clinical signs are usually limited to slightly decreased food intake in the intragastric dosing method. No clinical responses noted in the dietary method. Serum alkaline phosphatase levels do increase a little later, but other measurements remain normal until the tumor is well advanced and signs of liver failure are visible. Aflatoxin B_1 liver tumors are multicentric hepatocellular carcinomas without cirrhosis or significant fibrosis. Tumor nodules are soft, friable, and yellowish gray. Hemorrhage and necrosis are present in more advanced lesions. A trabecular pattern is often observed microscopically, but anaplastic types occur. Tumor extension to the mesentery and peritoneum is often seen, and metastasis to the lung is common. Bile duct hyperplasia, parenchymal cell damage, necrosis, and megalocytosis are prominent early lesions, but usually regress. Focal hyperplasia of basophilic parenchymal cells and foci of large, pale eosinophilic cells are seen, followed by nodule formation and liver cell carcinoma. One notable difference between the rat model and man is the absence of cirrhosis in the former.

5660 OBSERVATIONS ON THE RELATIONSHIP OF HEPATIC CHOLINE UPTAKE TO ETHANOLIC FATTY LIVER IN THE RAT.

(E.) Mendenhall, C. L.; Wilson, N. L. (VA Hosp., Cincinnati, Ohio). *Can. J. Biochem.* 51(7):1010-1013, 1973.

This study was undertaken to evaluate the effects of acute ethanol ingestion on hepatic choline requirements and to test whether the increased uptake of choline observed after ethanol ingestion may indicate an increased requirement for lecithin to be used in lipoprotein formation which, in turn, is needed for the removal of excess hepatic neutral lipids. Mature male Holtzman rats given radiotagged choline were sacrificed at varying time intervals after subsequent acute ethanol (6 g/kg) ingestion. An increase both in hepatic radiotagged choline uptake (mean 146%) and total hepatic triglycerides (mean 285%) was observed. However, radiotagged choline uptake occurred very rapidly and was maximal at 2 hr whereas triglycerides accumulated more slowly with the greatest values seen at 16 hr when no ethanol effect on choline uptake was observed. From this it appeared unlikely that triglyceride accumulation and hence a need for greater lipoprotein formation is responsible for the increased choline uptake. This increased uptake reflects more closely the overall ethanol-induced stimulation of hepatic lipid synthesis which occurs at 2 hr than a causal relation to the development of the ethanolic fatty liver at 16 hr.

5661 BILE ACIDS. XXXVIII. CONVERSION OF 5α-CHOLESTANE-3β,7α-DIOL TO ALLO BILE ACIDS BY THE RAT.

(E.) Noll, B. W.; Doisy, Jr., E. A.; Elliott, W. H. (St. Louis Univ. Sch. Med., Mo.). *J. Lipid Res.* 14(4):385-390, 1973.

Bile was collected for 11 days from adult male rats, with cannulated bile ducts, that had received 0.90-0.92 mg of 5α-[4-^{14}C,3α-^{3}H]-cholestane-3β,7α-diol, i. p. Bile from the first 10 hr, containing 63% of the administered ^{14}C and 6% of the ^{3}H, was hydrolyzed, and the bile acids were separated by acetic acid partition chromatography. Allochenodeoxycholic and allocholic acids contained at least 20.6% and 48.6%, resp., of the ^{14}C retained in the biliary acids. Small amounts of ^{14}C (2.5% and 1.9%, resp.) were present in the 3β isomers of these acids, but the ^{3}H content totaled more than 1/2 of that found in the bile acid fraction. No evidence was obtained for presence of the large quantities of the allomuricholates.

5662 HEPATOCARCINOGENESIS AND THE APPEARANCE OF SERUM ALPHA-FETOPROTEIN IN MICE TREATED WITH EXTRACTS OF BARLEY GRAIN INFECTED WITH FUSARIUM

SPOROTRICHIOIDES. *(E.)* Akhmeteli, M. A.; Linnik, A. B.; Cernov, K. S. (Gamaleja Inst. Epidemiol. Microbiol., Acad. Med. Sci. USSR, Moscow, USSR). *Bull. WHO* 47(5):663-664, 1972.

Male and female F_1 C57 x CBA hybrid mice (97) were each given 0.5 ml of aqueous extract of barley grain infected with *F. sporotrichioides* through a stomach tube 5 times a week for 1 yr. Blood samples tested by gel-diffusion 15 months after the start of the experiment were all negative for alpha-fetoprotein (AFP). One month later a more sensitive immunoautoradiographic testing procedure was used on 49 mice and at that time 9 of the 10 animals with hepatomas were AFP-positive, while 12 of the 39 without hepatomas were AFP-positive. Similarly, 9 of 21 AFP-positive mice had hepatomas, while only 1 of 28 AFP-negative mice had a hepatoma. Thus a negative finding with this sensitive test is usually associated with absence of a hepatoma. The positive findings in so many animals without hepatoma suggests that the presence of AFP indicates an early event in tumorigenesis preceding the appearance of a demonstrable hepatoma. It is difficult to relate AFP to the effect of treatment with *F. sporotrichioides* extract, for the 2 tumor-bearing mice in the non-treated control group also gave positive AFP tests. These data do not support the suggestion that AFP does not appear in hepatocarcinogenesis due to mycotoxins.

5663 HISTONE PHOSPHORYLATION IN THE REGENERATING RAT LIVER INDEPENDENT OF DIURNAL RHYTHMICITY. *(E.)* Letnansky, K. (Inst. Cancer Res., Univ. Vienna, Austria). *Fed. Eur. Biol. Soc. Lett.* 32(2):270-272, 1973.

Male Sprague-Dawley rats were hepatectomized by removal of 2/3 of their liver. A group of sham-operated rats served as controls. Both groups received 1 ml $[^{32}P]$ orthophosphate i.p. 1 hr prior to sacrifice. Maximum phosphorylation of individual histone fractions occurred 1, 2, 6, or 12 hr after partial hepatectomy. A general stimulation, affecting all histone fractions, was observed 22-30 hr after hepatectomy. Each phosphorylation maximum in the F2a, F2b, and F3 fractions required a corresponding maximum in the F1 group, suggesting a correlation between derepression and decondensation reactions. Administration of 3',5'-AMP also stimulated phosphorylation of F1 and other histone compounds. Except for F2a2, no influence of 3',5'-AMP injections on specific activity was found for the 12 hr interval, suggesting that maximum stimulation had directly been achieved by 3',5'-AMP concentrations.

5664 HORMONAL MODIFICATION OF MOUSE LIVER LYSOSOMAL PROTEIN METABOLISM BY CORTISONE ACETATE. *(E.)* Chertow, B. S.; Buchanan, W. E.; Mayron, M. S.; Schwartz, T. B. (VA West Side Hosp., Chicago, Ill.). *Endocrinology* 92(3):722-727, 1973.

The effect of cortisone acetate on hepatic lysosomal protein metabolism and its relation to stabilization of the lysosomal membrane were studied in white male mice. Denatured iodinated (^{125}I) human serum albumin (IHSA) was injected by tail vein, and large granule fractions containing lysosomes were isolated and incubated at pH 7 and 37 C for 1 hr in room air. The uptake of serum albumin was determined by measuring the total counts present in the lysosomal fractions and degradation was determined by measuring the trichloroacetic acid-soluble counts present immediately after sacrifice and released during incubation. Mice pretreated with a single injection of cortisone acetate (5 mg i.p. 2 hr prior to sacrifice) showed no significant change in uptake or degradation of the iodinated serum albumin. Mice pretreated with cortisone acetate (5 mg i.p.) in 3 equally spaced injections the day before and 2 hr prior to sacrifice showed a 32% increase in degradation *in vitro*. Mice pretreated with cortisone acetate (5 mg i.p.) daily for 4 days showed a 23% increase in degradation *in vitro*, a 29% increase in degradation *in vivo*, and a 73% increase in serum albumin uptake. Although vitamin A, a lysosomal disrupting agent, decreased IHSA degradation, cortisone acetate did not antagonize the effect of vitamin A. Hydrocortisone, 3.6 x 10^{-3}M *in vitro*, did not increase IHSA breakdown. Cortisone acetate did not decrease the nonsedimentable catheptic activity determined immediately after sacrifice. Thus, a catabolic effect of cortisone acetate on mouse liver protein metabolism is mediated through the lysosome but is not associated with membrane stabilization, although the integrity of the lysosomal membrane is necessary for optimal lysosomal catheptic activity.

5665 SYNTHETIC ACTIVITY OF ISOLATED RAT LIVER NUCLEI. II. EVIDENCE FOR PROTEIN FORMATION. *(E.)* Laval, M.; Bouteille, M. (Inst. Res. Sci. Cancer, Villejuif, France). *Exp. Cell Res.* 79(2):391-403, 1973.

5666 THE EFFECTS OF STARVATION AND REFEEDING ON CARBOHYDRATE AND LIPID METABOLISM IN VIVO AND IN THE PERFUSED RAT LIVER. THE RELATIONSHIP BETWEEN FATTY ACID OXIDATION AND ESTERIFICATION IN THE REGULATION OF KETOGENESIS. *(E.)* McGarry, J. D.; Meier, J. M.; Foster, D. W. (Univ. Texas Southwestern Med. Sch., Dallas). *J. Biol. Chem.* 248(1):270-278, 1973.

5667 EFFECT OF INTRADUODENAL GLUCOSE ADMINISTRATION ON HEPATIC EXTRACTION OF INSULIN IN THE ANESTHETIZED DOG. *(E.)* Kaden, M.; Harding, P.; Field, J. B. (Univ. Pittsburgh Sch. Med., Pa.). *J. Clin. Invest.* 52(8):2016-2028, 1973.

5668 EFFECT OF ACTIVATION OF α AND β ADRENERGIC RECEPTORS ON THE HEPATIC CELL MEMBRANE POTENTIAL IN PERFUSED DOG LIVER. *(E.)* Lambotte, L. (Lab. Exp. Surg., Univ. Louvain, Belgium). *J. Physiol.* 232(1):181-192, 1973.

5669 ISOLATION AND CHARACTERIZATION OF CORTISOL METABOLITES FROM LIVER OF ADRENALECTOMIZED RATS. *(E.)* Tsong, Y. Y.; Koide, S. S. (Biomed. Div., Population Council, Rockefeller Univ., New York, N.Y.). *J. Steroid Biochem.* 4(3):239-248, 1973.

5670 GLYCOGEN MOBILIZATION AFTER PARTIAL HEPATECTOMY. BIOCHEMICAL AND ULTRASTRUCTURAL STUDIES. *(E.)* Verity, M. A.; Travis, G.; Brown, W. J. (Ctr. Health Sci., Univ. California, Los Angeles). *Lab. Invest.* 27(1):108-114, 1972.

5671 RIBONUCLEASE ACTIVITY IN LIVER NUCLEI OF AFLATOXIN-TREATED RATS. *(E.)* Edwards, G. S.; Wogan, G. N. (Dept. Nutr. Food Sci., Massachusetts Inst. Tech., Cambridge). *Life Sci. (II)* 11(14):685-689, 1972.

5672 THE EFFECT OF RIBOFLAVIN DEFICIENCY ON KEY GLUCONEOGENIC ENZYME ACTIVITIES IN RAT LIVER. *(E.)* Garthoff, L. H.; Garthoff, S. K.; Tobin, R. B.; Mehlman, M. A. (Univ. Nebraska Coll. Med., Omaha). *Proc. Soc. Exp. Biol. Med.* 143(3):693-697, 1973.

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5674 EFFECT OF X-IRRADIATION AND FASTING ON HEPATOTOXICITY OF CARBON TETRACHLORIDE IN RATS. *(E.)* Highman, B.; Cyr, W. H.; Streett, Jr., R. P. (Armed Forces Inst. Pathol., Washington, D.C.). *Radiat. Res.* 54(3):444-452, 1973.

5675 COMPARISON OF PERFUSATES IN THE STUDY OF CHOLINE UPTAKE BY ISOLATED RAT LIVERS. *(E.)* Tuma, D. J.; Sorrell, M. F.; Barak, A. J. (Univ. Nebraska Med. Ctr., Omaha). *Res. Commun. Chem. Pathol. Pharmacol.* 6(1):345-348, 1973.

5676 THE INFLUENCE OF A GANGLION-BLOCKING AGENT ON EXPERIMENTAL LIVER INJURY. *(E.)* Kulcsar-Gergely, J.; Kulcsar, A. (Univ. Med. Sch., Debrecen, Hungary). *Toxicology* 1(2):125-130, 1973.

5677 ULTRASTRUCTURAL CHANGES IN RAT HEPATOCYTES FOLLOWING DISCONTINUATION OF PREGNENOLONE-16α-CARBONITRILE TREATMENT. *(E.)* Garg, B. D.; Tuchweber, B.; Werringloer, J.; Khandekar, J. D.; Kovacs, K. (Inst. Exp. Med. Surg., Univ. Montreal, Canada). *Acta Anat. (Basel)* 85(2):190-205, 1973.

5678 METABOLISM OF FRUCTOSE IN LIVER. *(E.)* Heinz, F. (Hanover Med. Coll., Germany). *Acta Med. Scand.* (Suppl. 542):27-36, 1972.

5679 HEPATIC ACCUMULATION OF METABOLITES AFTER FRUCTOSE LOADING. *(E.)* Woods, H. F. (Radcliffe Infirm., Oxford, England). *Acta Med. Scand.* (Suppl. 542):87-103, 1972.

5680 THE EFFECT OF INSULIN ON EPINEPHRINE AND GLUCAGON INACTIVATED GLYCOGEN SYNTHETASE I IN THE ISOLATED PERFUSED RAT LIVER. *(E.)* Hostmark, A. T. (Inst. Med. Biochem., Univ. Oslo, Norway). *Acta Physiol. Scand.* 88(2):248-255, 1973.

5681 PREVENTION OF GALACTOSAMINE-INDUCED LIVER CELL NECROSIS BY URIDINE. *(E.)* Farber, J. L.; Gill, G.; Konishi, Y. (Temple Univ. Sch. Med., Philadelphia, Pa.). *Am. J. Pathol.* 72(1):53-62, 1973.

5682 THE EFFECT OF ALIPHATIC AND HETEROCYCLIC MERCAPTO COMPOUNDS ON LIPID PEROXIDATION IN LIVER INJURY OF THE RAT BY CCl_4. *(Ger.)* Rauen, H. M.; Schriewer, H.; Tegtbauer, U.; Lasana, J. E. (Inst. Physiol. Chem., Univ. Munster, Germany). *Arzneim. Forsch.* 23(1a):145-149, 1973.

5683 INTRACELLULAR DISTRIBUTION OF SERUM ALBUMIN AND ITS POSSIBLE PRECURSORS IN RAT LIVER. *(E.)* Geller, D. M.; Judah, J. D.; Nicholls, M. R. (Univ. Coll. Hosp. Med. Sch., London, England). *Biochem. J.* 127(5):865-874, 1972.

5684 EFFECT OF PHENOBARBITAL INDUCTION ON GALACTOSE ELIMINATION CAPACITY IN THE RAT. *(E.)* Keiding, S.; Andreasen, P. B.; Fauerholdt, L. (Rigshosp., Copenhagen, Denmark). *Biochem. Pharmacol.* 22(8):2293-2297, 1973.

5685 BIOCHEMICAL EFFECTS OF CUPRIZONE ON MOUSE LIVER AND HEART MITOCHONDRIA. *(E.)* Hoppel, C. L.; Tandler, B. (Dept. Pharmacol., Case Western Reserve Univ., Cleveland, Ohio). *Biochem. Pharmacol.* 22(8):2311-2318, 1973.

5686 INFLUENCE OF AFLATOXIN B_1 AND AFLATOXIN B_2 ON RAT LIVER LYSOSOMAL ACID DEOXYRIBONUCLEASE. *(E.)* Pitout, M. J.; Schabort, J. C. (Natl. Res. Inst. Nutr. Dis., Pretoria, South Africa). *Biochem. Pharmacol.* 22(14):1801-1805, 1973.

5687 AN ABNORMALITY OF HEPATIC LIPOGENESIS IN A MUTANT STRAIN OF ACATALASEMIC MICE. *(E.)* Cuadrado, R. R.; Bricker, L. A. (Dept. Med. Technol., Florida Int. Univ., Miami). *Biochim. Biophys. Acta* 306(2):168-172, 1973.

5688 MICROSOMAL DESATURATION OF LINOLEIC INTO GAMMA-LINOLENIC ACID IN LIVERS OF FETAL, SUCKLING AND PREGNANT RATS. *(E.)* Satomi, S.;

Matsuda, I. (Sch. Med., Hokkaido Univ., Sapporo, Japan). *Biol. Neonate* 22(1-2):1-8, 1973.

5689 ROLE OF THE LIVER IN THE MECHANISM OF REDUCTION OF BLOOD SEROTONIN CONCENTRATION DURING ACUTE RADIATION SICKNESS. *(E.)* Dorofeev, V. M.; Zyablitsky, V. M.; Soboleva, E. L.; Nestaiko, G. V. (Res. Inst. Med. Radiol., USSR Acad. Med. Sci., Obninsk). *Biull. Eksp. Biol. Med.* 75(1):33-34, 1973.

5690 DISTURBANCES OF MICROCIRCULATION AND OF THE VASO-TISSUE PERMEABILITY IN ACUTE DIFFUSE EXPERIMENTAL HEPATITIS. *(E.)* Chernukh, A. M.; Kovalenko, N. Y. (Inst. Normal Pathol. Physiol., USSR Acad. Med. Sci., Moscow). *Biull. Eksp. Biol. Med.* 75(5):12-15, 1973.

5691 THE CONVERSION OF THE PYRROLIZIDINE ALKALOID TO PYRROLIC DERIVATIVES IN VIVO AND IN VITRO AND ITS ACUTE TOXICITY TO VARIOUS ANIMAL SPECIES. *(E.)* White, I. N. H.; Mattocks, A. R.; Butler, W. H. (Med. Res. Council Lab., Carlshalton, England). *Chem. Biol. Interact.* 6(4):207-218, 1973.

5692 EFFECTS OF FORMAMIDOXINE ON MACROMOLECULAR SYNTHESIS IN REGENERATING LIVER AND HEPATOMAS. *(E.)* Lea, M. A.; Khalil, F. L.; Rey, M. I.; Morris, H. P. (New Jersey Med. Sch., Newark). *Chem. Biol. Interact.* 6(6):339-349, 1973.

5693 SPECTROFLUORIMETRIC DETERMINATION OF INDIVIDUAL BILE ACIDS IN BIOLOGICAL FLUIDS: PERIPHERAL PLASMA. *(E.)* Feher, T.; Papp, J.; Kazik, M. H. (Semmelweis Univ. Med. Sch., Budapest, Hungary). *Clin. Chim. Acta* 44(3):409-418, 1973.

5694 PHYSIOLOGICAL FACTORS INFLUENCING INSULIN CLEARANCE BY THE ISOLATED PERFUSED RAT LIVER. *(E.)* McCarroll, A. M.; Buchanan, K. D. (Dept. Med., Queen's Univ., Belfast, Ireland). *Diabetologia* 9(3):174-177, 1973.

5695 HISTAMINE RELEASE DURING ORTHOTOPIC HOMOLOGOUS LIVER TRANSPLANTATION IN PIGS. *(E.)* Lorenz, W.; Hell, E.; Boecki, O.; Reimann, H. J.; Zimmermann, G.; Seidel, W.; Laszcz, M.; Uhlig, R. (Dept. Surg., Univ. Marburg, Germany). *Eur. Surg. Res.* 5(1):11-20, 1973.

5696 INHIBITION OF LIPOGENESIS IN RAT LIVER BY (-)-HYDROXYCITRATE. *(E.)* Sullivan, A. C.; Hamilton, J. G.; Miller, O. N.; Wheatley, V. R. (Hoffman-La Roche Inc., Nutley, N.J.). *Arch. Biochem. Biophys.* 150(1):183-190, 1972.

5697 POTENTIATION OF CCl_4-INDUCED HEPATOTOXICITY IN THE DOG BY CHRONIC EXPOSURE TO PHENOBARBITAL. *(E.)* Litterst, C. L.; Farber, T. M.; Van Loon, E. J. (Special Pharmacol. Animal Lab., FDA, Washington, D.C.). *Toxicol. Appl. Pharmacol.* 25(3):354-362, 1973.

5698 ELECTRON MICROSCOPIC OBSERVATIONS ON THE MUCOUS SECRETORY ACTIVITY OF THE HUMAN GALLBLADDER EPITHELIUM. *(E.)* Koga, A. (Kyushu Univ. Fac. Med., Fukuoka, Japan). *Z. Zellforsch.* 139(4):463-471, 1973.

5699 THE BEHAVIOR OF THE ISOLATED PERFUSED RAT LIVER AFTER POISONING WITH GALACTOSAMINE. *(Ger.)* Miertsch, H. J.; Roka, L. (Inst. Clin. Chem., Justus Liebig Univ., Giessen, Germany). *Z. Klin. Chem. Klin. Biochem.* 10(9):420-424, 1972.

See also, 5551, 5627, 5731, 5740, 5897, 5968, 6041.

Intestine

5700 HEXOKINASE ACTIVITY OF RAT INTESTINAL MUCOSA: DEMONSTRATION OF FOUR ISOZYMES AND OF CHANGES IN SUBCELLULAR DISTRIBUTION WITH FASTING AND REFEEDING. *(E.)* Anderson, J. W.; Tyrrell, J. B. (VA Hosp., San Francisco, Calif.). *Gastroenterology* 65(1):69-76, 1973.

The isozyme composition and subcellular distribution of hexokinase were studied in rat intestinal mucosa. Only 19% of total jejunal hexokinase was in the supernatant fraction whereas 44% of ileal activity was soluble. Cellulose acetate electrophoresis of intestinal mucosal supernatant fractions yielded 4 isozymes, including glucokinase. The type IV isozyme in intestine closely resembled hepatic glucokinase; only intestine and liver appear to contain this specific isozyme. Feeding rats a 75% glucose diet increased hexokinase activity of the particulate fraction of jejunal mucosa by 25% but increased the supernatant activity by only 12%. Alterations in the intracellular distribution of hexokinase were seen more clearly when serial time studies were done in fasted, glucose-refed rats. Refeeding was associated with a specific increase, seen at days 1 and 2, in particulate activity which doubled, without changes in supernatant activity. After 5 days of refeeding, however, comparable increases in particulate and supernatant fractions had occurred. These studies indicate that the adaptive responses of jejunal mucosa to dietary change include specific changes in the intracellular compartmentation of hexokinase. The changes in subcellular distribution of hexokinase may be of importance in the regulation of glucose metabolism in the intestine.

5701 REGULATORY EFFECTS OF DIETARY STEROLS AND BILE ACIDS ON RAT INTESTINAL HMG CoA REDUCTASE. *(E.)* Shefer, S.; Hauser, S.; Lapar, V.; Mosbach, E. H. (Public Health Res. Inst. New York, N.Y.). *J. Lipid Res.* 14(4):400-405, 1973.

The specific activity (concentration) of microsomal 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase of intestinal crypt cells was measured in male Wistar rats fed sterols and bile acids, either singly or in combination. The basal activity of the reductase was not suppressed by administration of relatively large amounts (about 200 mg/rat/day) of bile acid (taurocholate or taurochenodeoxycholate). Bile acids reduced the specific activity of the reductase only in rats in which enzyme activity had first been enhanced by biliary diversion or by 2% sitosterol feeding. In addition, bile acid feeding abolished the 70% elevation of reductase activity that normally occurs between midnight and 2 a.m. In no case did bile acids reduce enzyme activity below basal levels. A 60% reduction of intestinal HMC CoA reductase activity was observed in rats fed diets containing 2% cholesterol combined with 1% bile acid. This reduction in activity was not due to increased intestinal bile acid flux but was associated with increased sterol concentrations within the intestinal crypt cells. Thus, dietary sterols and bile acids both play a role in the regulation of intestinal HMG CoA reductase.

5702 INTESTINAL METABOLISM OF FRUCTOSE. *(E.)* Herman, R. H.; Stifel, F. B.; Greene, H. L.; Herman, Y. F. (Fitzsimons Gen. Hosp., Denver, Col.). *Acta Med. Scand.* (Suppl. 542):19-25, 1972.

5703 STUDIES OF INTESTINAL AND FAECAL SUBSTANCES FROM GERMFREE RATS INHIBITING BACTERICIDAL ACTIVITY OF RAT SERUM. *(E.)* Winsnes, R.; Trippestad, A.; Midtvedt, T.; Wold, J. K. (Dept. Pharmacog., Univ. Oslo, Norway). *Acta Pathol. Microbiol. Scand. (B)* 81(2):223-241, 1973.

5704 FOLATE DEFICIENCY OF THE INTESTINAL MUCOSA. *(E.)* Klipstein, F. A.; Lipton, S. D.; Shenk, E. A. (Univ. Rochester Sch. Med., N.Y.). *Am. J. Clin. Nutr.* 26(7):728-737, 1973.

5705 PLASMA MEMBRANE AND MUCOSAL GLYCOSPHINGOLIPIDS IN THE RAT INTESTINE. *(E.)* Forstner, G. G.; Wherrett, J. R. (Inst. Med. Sci., Univ. Toronto, Canada) *Biochim. Biophys. Acta* 306(3):446-459, 1973.

5706 DISTRIBUTION AND REGULATION OF DEOXYTHYMIDINE KINASE ACTIVITY IN DIFFERENTIATING CELLS OF MAMMALIAN INTESTINES. *(E.)* Salser, J. S.; Balis, M. E. (Sloan-Kettering Inst. Cancer Res., New York, N.Y.). *Cancer Res.* 33(8):1889-1897, 1973.

5707 pH IN THE HUMAN DUODENUM. ITS PHYSIOLOGICAL AND PATHOPHYSIOLOGICAL SIGNIFICANCE. *(E.)* Rune, S. J. (Gentofte Hosp., Copenhagen, Denmark). *Digestion* 8(3):261-268, 1973.

5708 RECEPTORS OF 1,25-DIHYDROXYCHOLECALCIFEROL IN RAT INTESTINE. *(E.)* Chen, T. C.; DeLuca, H. F. (Dept. Biochem., Univ. Wisconsin, Madison). *J. Biol. Chem.* 218(14):4890-4895, 1973.

5709 PREPARATION AND CHARACTERIZATION OF MOUSE INTESTINAL PHOSPHOLIPASE. *(E.)* Ottolenghi, A. (Duke Med. Ctr., Durham, N.C.). *Lipids* 8(7):415-425, 1973.

5710 LOWERING OF SERUM CHOLESTEROL BY INTESTINAL BACTERIA IN CHOLESTEROL-FED PIGLETS. *(E.)* Mott, G. E.; Moore, R. W.; Redmond, H. E.; Reiser, R. (Dept. Pathol. Biochem., Univ. Texas Med. Sch., San Antonio). *Lipids* 8(7):428-431, 1973.

711 SMALL INTESTINE CARBOHYDRASE ACTIVITIES IN
EXPERIMENTAL SALMONELLA ENTEROCOLITIS IN
ICE. *(E.)* Madge, D. S. (Dept. Biol. Sci., Wye
oll., Kent, England). *Life Sci. (II)* 12(12):
35-542, 1973.

See also, 5528, 5562, 5625, 5667, 5930.

GENERAL

12 THE ORIGIN, HORMONAL NATURE, AND ACTION OF
HEPATOTROPHIC SUBSTANCES IN PORTAL VENOUS
OOD. *(E.)* Starzl, T. E.; Francavilla, A.; Hal-
imson, C. G.; Francavilla, F. R.; Porter, K. A.;
own, T. H.; Putnam, C. W. (VA Hosp., Denver,
lo.). *Surg. Gynecol. Obstet.* 137(2):179-199,
73.

atomic and biochemical investigations were under-
ken on dogs to determine the source and mechanism
the hepatotrphic factors in splanchnic venous
ood. Experimentally, either the left or the right
rtal vein was detached from the main portal trunk
33 dogs and revascularized to the supra-adrenal
ferior vena cava. Thus one compartment of the
ver received portal splanchnic venous blood and
e other, blood from kidneys, adrenals, and hind-
arters. In 8 other dogs, the systemic venous
ood was derived from the infrarenal inferior vena
va. In an additional group, one side of the liver
ceived portal blood of an intestinal source, and
e other side received venous blood returning from
e pancreatic, splenic, and gastroduodenal beds.
additional 9 dogs underwent portacaval transposi-
on, and 5 others had a modified portacaval trans-
sition, minus adrenal and renal inflow. Liver
es receiving splanchnic venous inflow had in-
eased in weight after 2 1/2 months and had
ikingly hypertrophic hepatocytes, whereas liver
lls shrank in lobes perfused with vena caval blood.
cogen and glucokinase were more prominent in lobes
plied with splanchnic venous blood and there was
dence of hyperplasia. In the split transposition
luding adrenal and renal blood, the morphology was
ilar at 9 weeks, but less marked changes occurred
n with regular split transposition. Hyperplasia
weight gain occurred in lobes receiving pancrea-
, gastroduodenal, and splenic blood. Dogs with
ventional and modified portacaval transposition
hepatic deglycogenation and striking elevations
cyclic 3',5'-adenosine monophosphate. The rate
cyclic 3',5'-adenosine monophosphate formation
greater in liver tissue receiving vena caval
n that receiving splanchnic venous blood. A
e rapid rate of cyclic 3',5'-adenosine monophos-
te synthesis occurred in lobes receiving splenic-
troduodenal-pancreatic-rather than intestinal
od. These results indicate that the hepatotrophic
tor found in splanchnic venous blood are pancreatic
mones, i.e., insulin and glucagon.

5713 PRELIMINARY REPORT. FIXATION AND INACTIVATION OF CHOLERA TOXIN BY G_{M1} GANGLIOSIDE. *(E.)* Holmgren, J.; Lonnroth, I.; Svennerholm, L. (Inst. Med. Microbiology, Univ. Goteborg, Sweden). *Scand. J. Infect. Dis.* 5(1):77-78, 1973.

The effect of a number of pure gangliosides and related neutral glycosylceramides on isolated cholera toxin was analyzed to identify the structure of the receptor. In contrast to all other gangliosides or neutral glycolipids tested, G_{M1} ganglioside, fixed toxin *in vitro*. The minimal amount of G_{M1} required for a precipitation line was 25 ng. A line was also achieved with toxoid; 100 ng of G_{M1} was required. Toxin was also inactivated, although inconsistently, with G_{A1} and G_{D1a}. In skin tests the toxin was inactivated only by the same gangliosides: with 5 ng toxin 100 pg G_{M1}, 100 ng G_{A1}, or 100 ng G_{D1a} was required for activation. Since the data showed the existence of specific binding in 1:1 stoichiometric proportions for G_{M1} to toxin, it suggests that G_{M1} ganglioside could be the tissue receptor for cholera toxin. It is possible that the inactivation of toxin caused by high concentrations of G_{A1} and G_{D1a} may be due to some affinity of the toxin for these compounds with neutral carbohydrate chains indentical to that of G_{M1}. Sialidase might also convert G_{D1a} to G_{M1} *in vivo*.

5714 POSTERIOR HYPOTHALAMIC EFFECT ON GASTROINTESTINAL BLOOD FLOW IN THE CONSCIOUS CAT. *(E.)* Gilsdorf, R. B.; Urdaneta, L. F.; Leonard, A. S.; Delaney, J. P. (Minneapolis VA Hosp., Minn.). *Proc. Soc. Exp. Biol. Med.* 143(2):329-334, 1973.

Cats receiving posterior hypothalamic stimulation had significantly less blood flow to the colon mucosa (51%), submucosa (60%), and muscularis (57%) and to small intestinal mucosa (70%) than control cats. There was no significant difference in blood flow to the tissues of the esophagus, stomach, gallbladder, or pancreas. Cardiac output was not different in the 2 groups despite significant increases in blood pressure (147%) and pulse (127%) in stimulated animals. Tissue blood flows in the control group ranged from the high in the pancreas of 1.36 ml/g/min followed by the colon, duodenum, jejunum, ileum, and gastric corpus to the low in the gastric antrum of 0.54 ml/g/min. It is concluded that posterior hypothalamic stimulation can affect tissue blood flow in the gastrointestinal organs but the magnitude of the change is not sufficient to provide the sole explanation for reported physiologic and pathologic changes associated with such stimuli.

5715 ADDITIONAL STUDIES ON THE NATURE OF BIG BIG GASTRIN.

(E.) Yalow, R. S.; Wu, N. (VA Hosp., Bronx, N.Y.). *Gastroenterology* 65(1):19-27, 1973.

Electrophoresis, ultracentrifugation, and gel filtration were used in the analysis of a new form of immunoreactive gastrin called "big big gastrin." This component elutes in the void volume of Sephadex G-50 gel filtration, has the same ultracentrifugal sedimentation velocity as human growth hormone, and an electrophoretic mobility on starch gel just in advance of serum albumin. Trypsin converts big big gastrin to smaller hormonal forms down to and including heptadecapeptide-like gastrin. Big big gastrin is a major fraction of total gastrin immunoreactivity in normal human, canine, and porcine plasmas in the nonstimulated state and is the only form detectable in a patient after Billroth II gastroenterostomy. It is not detectably stimulated by feeding and comprised less than about 2% of the total immunoreactivity in a Zollinger-Ellison tumor or in the plasma of patients with Zollinger-Ellison syndrome, pernicious anemia, or gastrin hypersecretion. Its biologic significance has not as yet been evaluated. A family of immunoreactive gastrins with elution volumes between the new component and the previously described big gastrin has been detected as a minor component of an extract of a Zollinger-Ellison tumor and after tryptic digestion of big big gastrin. It has not been determined whether this family of gastrins is significant *in vivo* or simply represents degradation products of this new component.

5716 PEPSIN INHIBITORY ACTIVITY AMONGST ACTIVATION PEPTIDES OF PEPSINOGEN.

(E.) Anderson, W.; Harthill, J. E. (Dept. Pharm. Technol., Univ. Stratchlyde, Glasgow, Scotland). *Nature (Lond.)* 243(5407):417-419, 1973.

A study was made of the peptides separated by a chromatographic method after release from porcine pepsinogen activated at pH 2 for 1 min. One of the peptides (AP-V) has pepsin inhibitory activity equivalent to the inhibitory activity of pepsin inhibitor at pH 5.7 in the milk clotting system, but differs from pepsin inhibitor in its amino acid structure and in having fewer amino acid residues, although both have the same N-terminal amino acid, leucine. AP-V also has marked ninhydrin inhibitory activity. There appears to be less correspondence between pepsin inhibitor and pepsinogen than between AP-V and pepsinogen. Basic peptides, devoid of pepsin inhibitory activity, have also been eluted from porcine pepsinogen. This absence of pepsin inhibitory activity supports the contention that inhibitory interaction with pepsin at pH 5 to 6 requires in the peptide something more than the presence of basic amino acid residues.

5717 THE EFFECTS OF VASOCONSTRICTOR FIBRE STIMULATION ON CONSECUTIVE VASCULAR SECTIONS OF CAT SMALL INTESTINE DURING HEMORRHAGIC HYPOTENSION.

(E.) Haglund, U.; Lundgren, O. (Dept. Physiol., Univ. Goteborg, Sweden). *Acta Physiol. Scand.* 88(1):95-108, 1973.

Using a plethysmographic technique, the effects of the regional sympathetic vasoconstrictor fibers on the consecutive vascular sections of the small intestine of the cat were studied during 2-2.5 hr hemorrhagic hypotension. The constrictor fibers were intermittently stimulated at 4 Hz before, during, and after a hypotensive period at approximately 60 or 40 mm Hg. The nervous responsiveness of the resistance vessels and of the capacitance vessels declined continuously throughout the hypotensive period, the rate of decline increasing with decreasing perfusion pressure and decreasing arterial blood pH. The capillary filtration coefficient, reflecting the tonus of the "precapillary sphincters", was increased during the hypotensive period. Nervous activation reduced the capillary filtration coefficient throughout the experiments. Tissue volume increased continuously during the latter half of most experiments at 40 mm Hg, probably reflecting a deranged Starling equilibrium across the capillary wall. During the post-hypotensive control period after 40 mm Hg hypotension, arterial blood pressure fell rapidly. Mucosal ulcerations were regularly found in these animals. A mechanism for the pathogenesis of ulcerations is suggested which implies that oxygen tension is low in the villous tips due to extravascular short-circuiting of the gas at the bases of the villi. In a hypotensive state the intestinal countercurrent exchanger may be even more efficient. This would greatly increase the changes of extravascular oxygen short-circuiting and it might result in a degree of villous hypoxia severe enough to cause cell death in the tips.

5718 MECHANISMS OF DISSOLUTION OF HUMAN CHOLESTEROL GALLSTONES.

(E.) Higuchi, W. L.; Prakongpan, S.; Young, F. (Coll. Pharmacy, Univ. Michigan, Ann Arbor). *J. Pharm. Sci.* 62(6): 945-948, 1973.

Experiments were designed for investigating and comparing the *in vitro* dissolution kinetics of human cholesterol gallstones and cholesterol monohydrate compressed pellets. The dissolution rates were determined in 66% acetone-water, in 63% ethanol-water, in bile acids, and in bile acid-lecithin solutions. The rates of dissolution of the stones compared well with the dissolution rates obtained with the cholesterol monohydrate pellets in all solvents investigated. The dissolution rates for both stones and pellets in the organic-aqueous solvents were extremely rapid, e.g., 2.60 mg/cm^2/sec for ethanol-water, and of the order of magnitude expected for a bulk diffusion-controlled process. In sodium

iolate solutions, the dissolution rates were about
-3 times slower than rates predicted by diffusion
ieory, e.g., 0.67 $mg/cm^2/sec$ for 2% cholate, and
ie data suggested a modest interfacial resistance
dissolution. The rates obtained in 2% bile
id-1% lecithin solutions were about 17 times
ower, e.g., 0.075 $mg/cm^2/sec$ for taurocholate,
ian lecithin diffusion-controlled processes, indi-
iting that a very large interfacial barrier clearly
minates the kinetics and might be very important
inically.

'19 PURIFICATION AND PROPERTIES OF ONE OF THE MULTIPLE FORMS OF PEPTIDE HYDROLASES FROM
IINEA-PIG INTESTINAL MUCOSA. *(E.)* Donlon, J.;
ttrell, P. F. (Univ. Coll. Galway, Ireland).
ochem. Soc. Trans. 1(1):250-252, 1973.

e 'α' peptide hydrolase from guinea-pig intestinal
cosa was separated from other peptide hydrolases
chromatography. Examination by starch-gel
ectrophoresis revealed the hydrolase to be com-
etely free of the other peptide hydrolases present
the original extract. The enzyme also lacked
dopeptidase activity and carboxypeptidase A
tivity. The enzyme was extremely active with the
llowing substrates: Leu-L-Leu, L-Leu-L-Leu-L-Leu,
Leu-Gly, and L-Leu-Gly-Gly. Molecular weight was
0,000. In regard to whether peptide hydrolase
tivity, against the same peptide, in brush-border
d cytosol fractions of the enterocyte is due to
fferent enzymes, the small amount of 'α' peptide
drolase activity in the brush-border fraction of
inea-pig intestinal mucosa also had a molecular
ight of 300,000. The activity of the enzyme was
imulated 3-fold by Mn^{2+}, slightly inhibited by
$^{2+}$ and Zn^{2+}, and not affected by Mg^{2+}. The
zyme was inhibited by ethylenediamine-tetraacetic
id, 8-hydroxyquinoline, *o*-phenanthroline, and
ethyldithiocarbamate.

20 AUTOREGULATORY ESCAPE IN THE GUT: A SYSTEMS ANALYSIS. *(E.)* Shepherd, A. P.; Granger,
J. (Univ. Texas Med. Sch., Houston). *Gastro-
terology* 65(1):77-91, 1973.

mathematical model of circulatory control in the
t was developed to determine whether a metabolic
edback mechanism could account for intestinal
toregulation and autoregulatory escape. The model
nsists of equations describing hemodynamics, oxygen
ansport, and local and nervous effects on mesenteric
teriolar and precapillary sphincter tone. It is
sumed tha the local system controls intracellular
ygen partial pressure by regulating arteriolar
sistance to change blood flow and by opening or
osing precapillary sphincters, thereby determining
pillary density (the number of open capillaries)
d the diffusion parameters (surface area and dif-
sion distance). Sympathetic activation increases
teriolar and precapillary spincter tone. The
del responded to step changes in arterial pressure
autoregulating blood flow to control oxygen delivery in computer simulations. The degree of autoregulation increased whenever the amount of extractable oxygen in the blood decreased. This has been observed experimentally in skeletal muscle but not yet in the intestine. In simulations of autoregulatory escape, sustained sympathetic activation caused a fall in mesenteric blood flow, capillary density, and oxygen delivery. Capillary density remained depressed, but blood flow and oxygen delivery returned toward control. The end of sympathetic activation was followed by hyperemia and an overshoot in capillary density. These results agree with those obtained experimentally. However, the model predicts that, as capillary density is depressed by the sympathetic input, the degree of autoregulatory escape and post-stimulation hyperemia will increase. The degree of autoregulation varied greatly with initial flow conditions, yet the escape index hardly changed. This finding could account for the failure of experimental attempts to correlate the degree of autoregulation with the degree of escape. It is concluded that the metabolic feedback hypothesis can adequately explain autoregulation and autoregulatory escape; however, a description complete enough to account for intestinal hemodynamics in some experimental conditions (e.g., venous pressure elevation) must also include certain myogenic properties of the intestinal vasculature.

5721 EFFECT OF GLUCAGON ON CIRCULATING GASTRIN. *(E.)* Becker, H. D.; Reeder, D. D.; Thompson, J. C. (Univ. Texas Med. Branch, Galveston). *Gastroenterology* 65(1):28-35, 1973.

The effect of glucagon on basal and food-stimulated gastrin release, measured by radioimmunoassay, was studied in 7 normal persons, 8 patients with duodenal ulcer, 6 patients with the Zollinger-Ellison syndrome, and 6 Heidenhain pouch dogs. Glucagon (30 μg/kg/hr, i.v.) diminished the basal serum gastrin values in normal persons (from 105 to 82 pg/ml) in duodenal ulcer patients (from 156 to 118 pg/ml), and in dogs (from 54 to 42 pg/ml). Gastric response to a standard meal was also diminished. In patients with the Zollinger-Ellison syndrome, glucagon caused an immediate increase in basal serum gastrin concentrations (from 4151 to 7947 pg/ml), and did not diminish the gastrin response to a meal. Lowering the glucagon dosage to 0.5 μg/kg/hr did not influence the inhibitory effect on basal values of gastrin or on stimulated gastrin release in normal persons. The effects of glucagon and gastrin are not related to the hyperglycemic effect of glucagon. These effects of glucagon on serum gastrin closely parallel the effects of secretin, and it is proposed that glucagon may be involved in the physiologic control of gastrin release.

5722 THE LIFE SPAN OF IgA PLASMA CELLS FROM THE MOUSE INTESTINE. *(E.)* Mattioli, C. A.; Tomasi, Jr., T. B. (Dept. Med., State Univ. New York, Buffalo). *J. Exp. Med.* 318(2):452-460, 1973.

Tritiated thymidine (15 μC) was injected (i.p. every

6 hr from day 15 to day 35 of age) into conventional CBA mice. The disappearance rate of tritium-labeled IgA plasma cells was followed by a technique combining immunofluorescence with autoradiography which permitted the identification of the immunoglobulin class of plasma cells with labeled nuclei. It was thus possible to calculate that the majority of intestinal IgA plasma cells have a half-life of 4.7 days under physiological conditions of stimulation. It is noted that this is an estimate of the renewal rate within the intestinal compartment rather than the true life span of the IgA cells. The maximum life span of both intestinal IgA plasma cells and the IgA, IgG, and IgM plasma cells from the spleen is of the order of 7-8 week.

5723 CRITICAL REVIEW OF METHODS FOR MEASURING LIVER BLOOD FLOW IN ANIMAL EXPERIMENTS AND HUMAN MEDICINE. *(Fr.)* Loisance, D. Y.; Lenriot, J. P. (Broussais Hosp., Paris, France). *Coeur Med. Interne* 11(3):547-557, 1972.

5724 LIVER BLOOD FLOW UNDER NORMAL AND PATHOLOGICAL CONDITIONS. *(It.)* Leggio, F. (Gen. Provincial Hosp., Rieti, Italy). *Fegato* 18(1):101-123, 1972.

5725 EFFECT OF SECRETIN, PANCREOZYMIN, HISTAMINE, AND DECHOLIN ON CANINE PANCREATIC BLOOD FLOW. *(E.)* Papp, M.; Varga, B.; Folly, G. (Inst. Exp. Med., Hungarian Acad. Sci., Budapest). *Pfleugers Arch.* 340(4):349-360, 1973.

5726 SALIVARECTOMY: EFFECT ON DRINKING PRODUCED BY ISOPROTERENOL, DIAZOXIDE AND NaCl LOADS. *(E.)* Falk, J. L.; Bryant, R. W. (Dept. Psychol., Rutgers Univ., New Brunswick, N.J.). *Pharmacol. Biochem. Behav.* 1(2):201-210, 1973.

5727 GLYCOGEN-ASSOCIATED PROTEINS OF RAT LIVER. *(E.)* Scott, R. B.; Cooper, L. W. (Med. Coll. Virginia, Richmond). *Proc. Soc. Exp. Biol. Med.* 143(3):862-863, 1973.

5728 RADIOIMMUNOASSAY FOR GASTRIN EMPLOYING IMMUNOSORBENT. *(E.)* Rehfeld, J. F.; Stadil, F. (Bispebjerg Hosp., Copenhagen, Denmark). *Scand. J. Clin. Lab. Invest.* 31(4):459-464, 1973.

5729 STUDY OF THE GASTRO-INTESTINAL MICROFLORA OF SUCKLING PIGLETS AND EARLY WEANED PIGLETS REARED USING DIFFERENT FEEDING SYSTEMS. *(E.)* Decuyprer, J.; Van der Heyde, H. (Dept. Nutr. Hyg., Univ. Ghent, Belgium). *Zentralbl. Bakteriol. (Orig. A)* 221(4):492-510, 1972.

5730 FAILURE OF ENDOGENOUS GASTRIN RELEASE TO AFFECT SERUM INSULIN. *(E.)* Budillon, G.; Mazzacca, G.; Squame, G. (Second Inst. Med. Clin., Univ. Naples, Italy). *Digestion* 8(3):201-207, 1973.

5731 METABOLIC OSCILLATIONS AND FOOD INTAKE. *(E.)* Allred, J. B.; Roehrig, K. L. (Dept. Food Sci. Nutr., Ohio State Univ., Columbus). *Fed. Proc.* 32(6):1727-1730, 1973.

5732 POTENCY OF STIMULANTS AND HALF-LIFE OF HORMONAL PEPTIDES IN SPECIES OF DIFFERENT BODY SIZE. *(E.)* Makhlouf, G. M. (Med. Coll. Virginia, Richmond). *Gastroenterology* 65(1):170-173, 1973.

5733 THE ROLE OF THE LIVER IN NON-SHIVERING THERMOGENESIS IN THE RAT. *(E.)* Stoner, H. B. (Med. Res. Council Lab., Carshalton, England). *J. Physiol.* 232(2):285-296, 1973.

5734 HIGH PHOSPHOLIPASE CONTENT OF INTESTINES OF MICE INFECTED WITH HYMENOLEPIS NANA. *(E.)* Ottolenghi, A. (Duke Med. Ctr., Durham, N.C.). *Lipids* 8(7):426-428, 1973.

5735 BIG GASTRIN. *(E.)* Gregory, R. A.; Tracy, H. J. (Physiol. Lab., Univ. Liverpool, England). *Mt. Sinai J. Med. N.Y.* 40(3):359-364, 1973.

5736 EXPERIMENTAL MODEL FOR PRODUCTION OF PERFORATING DUODENAL ULCERS BY CYSTEAMINE IN THE RAT. *(E.)* Selye, H.; Szabo, S. (Inst. Med. Exp. Surg., Univ. Montreal, Canada). *Nature* 244(5416):458-459, 1973.

5737 A SIMPLE METHOD FOR THE PRODUCTION OF PEPTIC ULCERATION IN THE RAT. *(E.)* Dai, S.; Ogle, C. W. (Fac. Med., Univ. Hong Kong). *Life Sci.* 12(Part 2):505-512, 1973.

5738 AN IMPROVED PROCEDURE FOR ISOLATING BILE SALTS. *(E.)* Smith, A.; Anderson, L. J.; Lough, A. K. (Rowett Res. Inst., Bucksburn, Aberdeen, England). *Chem. Ind.* (10):484, 1973.

5739 IS γ-CHYMOTRYPSIN AN AUTOLYTIC PRODUCT IN THE ACTIVATION SCHEME OF CHYMOTRYPSINOGEN A? *(E.)* Avery, M. J.; Hopkins, T. R. (Dept. Biochem., Univ. Otago, Dunedin, New Zealand). *Biochem. Biophys. Acta* 310(1):142-147, 1973.

5740 MAINTENANCE IN VITRO OF FUNCTIONALLY ACTIVE ADULT HUMAN LIVER. *(E.)* Sandstrom, B. (Dept. Human Anat., Univ. Uppsala, Sweden). *Acta Hepatogastroenterol.* 20(1):19-23, 1973.

5741 EFFECT ON SERUM LIPIDS OF DIETARY SUCROSE AND FRUCTOSE. *(E.)* Macdonald, I. (Guy's Hosp., London, England). *Acta Med. Scand.* (Suppl. 542):215-219, 1972.

5742 COPPER METABOLISM IN YOUNG WOMEN FED TWO-LEVELS OF COPPER AND TWO PROTEIN SOURCES. *(E.)* Butler, L. C.; Daniel, J. M. (Maryland Agr. Exp. Sta., College Park). *Am. J. Clin. Nutr.* 26(7): 744-749, 1973.

5743 RESPONSE OF INTRAHEPATIC VASCULATURE TO ISOPROTERENOL AND EPINEPHRINE INFUSIONS. *(E.)* Hanson, K. M. (Ohio State Univ. Coll. Med., Columbus). *Angiologica* 10(2):65-75, 1973.

5744 METABOLIC STUDIES OF [^{75}Se]SELENOMETHIONINE AND [^{75}Se]SELENITE IN THE RAT. *(E.)* Thomson, C. D.; Stewart, R. D. H. (Dept. Med., Univ. Otago, New Zealand). *Br. J. Nutr.* 30(1):139-147, 1973.

See Also, 5552.

DIAGNOSTIC PROCEDURES

5745 POSTPRANDIAL SERUM BILE ACID FOR THE DETECTION OF HEPATOBILIARY DISEASE. *(E.)* Kaplowitz, N.; Kok, E.; Javitt, N. B. (Cornell Univ. Med. Coll., New York, N.Y.). *J.A.M.A.* 225(3):292-293, 1973.

Fasting and 2-hr postprandial serum bile acid concentrations were measured with gas-liquid chromatography in 10 normal subjects (5 male and 5 female) and in 26 patients (18 male and 8 female) with a variety of hepatobiliary diseases including viral hepatitis (6), chronic hepatitis (4), biliary cirrhosis (4), cryptogenic cirrhosis (3), Laennec cirrhosis (2), partial biliary atresia (2), common duct stricture (1), pericholangitis associated with Crohn's disease (1), acute fatty liver (1), chlorpromazine hepatitis (1), and lymphomatous infiltration of the liver (1). The results of serum bile acid concentrations were compared with results from other liver function tests (BSP, alkaline phosphatase, 5'-nucleotidase, SGOT, SGPT, and serum bilirubin). The 2-hr postprandial serum bile acid determination was the only test that gave abnormal results in all 26 cases. In 10 patients abnormal postprandial serum bile acid values were associated with normal fasting levels, and all patients had at least a 70% increase in postprandial bile acids. There was no correlation between the increase in postprandial serum bile acid concentrations and severity of the hepatobiliary disease. It is concluded that a 2-hr postprandial serum bile acid is a sensitive screening test for hepatobiliary disorders.

5746 USE OF BARIUM IN THE DIAGNOSIS OF APPENDICITIS IN CHILDREN. *(E.)* Schey, W. L. (Michael Reese Hosp., Chicago, Ill.). *Am. J. Roentgenol. Radium Ther. Nucl. Med.* 118(1):95-103, 1973.

The barium enema examination was performed in 25 patients (aged 8 months to 19 yr) with appendicitis and in a group of patients without appendicitis. Findings in the barium enema study of non-filling of the appendix, plus a mass; non-filling of the appendix with associated findings; partial filling with and without a mass; and irregular filling or a "cut-off sign" are strongly suggestive, if not diagnostic, of acute appendicitis. Non-filling of the appendix occurs about 8% of the time and should be considered suspicious of an appendiceal problem. Plain film roentgenographic findings, other than an appendicolith or gas within the appendix, are inconclusive and cannot indicate the nature of the problem in as specific a manner as the barium enema examination. The barium enema examination is a harmless procedure in patients with acute appendicitis and its use is recommended.

5747 DRIP-INFUSION CHOLANGIOGRAPHY: A SECOND LOOK. *(E.)* Howland, W. J.; Rothermel, W. S.; Topcuoglu, H. N.; Avenido, M. M. (Aultman Hosp., Canton, Ohio). *Radiology* 107(1):71-73, 1973.

A double-blind study comparing cholangiograms obtained on 50 patients by conventional injection of iodipamide (20 ml, i.v.) with cholangiograms made on 127 patients after injection of iodipamide (40 ml) diluted in 250 ml 20% glucose in water infused over a one hr period was performed. In the group receiving the larger iodipamide dose there were 3 occurrences of urticaria and 3 of nausea. When technical factors were not changed, there was no significant difference in the visualization ratings. When technical factors were changed to include low voltage, routine tomography, precise collimation, and patient immobilization, there was marked improvement in visualization. It was concluded that technical factors are more important for good i.v. cholangiography than increasing the amount of contrast material or prolonging the injection time.

5748 COMBINED LIVER SCANNING AND FINE-NEEDLE PUNCTURE IN TUMOR DIAGNOSIS. *(Dan.)* Thommesen, P. (Central Hosp., Randers, Denmark). *Ugeskr. Laeg.* 134(35):1841-1844, 1972.

5749 POTASSIUM IODIDE TEST FOR EVALUATING SMALL INTESTINE ABSORPTION. *(Rus.)* Leshchinskii, L. A.; Plastinina, R. A.; Riabov, V. I.; Trusov, V. V. (Izhevsk Med. Inst., USSR). *Sovet. Med.* 35(7): 88-93, 1972.

5750 SIGNIFICANCE AND PRACTIBILITY OF NORMOTEST IN DIAGNOSIS OF CHRONIC LIVER DISEASES. *(E.)* Henning, H.; Yano, M. (Fohrenkamp Hosp., Molln/Lauenburg, Germany). *Scand. J. Gastroenterol.* [*Suppl.*] 8(19):119-123, 1973.

5751 IMMUNOGLOBULIN VALUES IN 6 CASES OF NEONATAL SALMONELLA TYPHIMURIUM ENTERITIS. *(It.)* Ceci, A.; Vavuraki, D.; Armenio, L. (Inst. Clin. Pediatr., Univ. Bari, Italy). *Minerva Pediatr.* 25(4):157-160, 1973.

5752 BEHAVIOUR OF ANTITHROMBIN III IN LIVER DISEASE. *(E.)* Duckert, F. (Canton Hosp., Basel, Switzerland). *Scand. J. Gastroenterol.* [*Suppl.*] 8(19):109-112, 1973.

5753 VALUE OF NORMOTEST AND ANTITHROMBIN III IN THE ASSESSMENT OF LIVER FUNCTION. *(E.)* Mannucci, L.; Dioguardi, N.; Del Ninno, E.; Mannucci, P. M. (Hosp. Policlin., Univ. Milan, Italy). *Scand. J. Gastroenterol.* [*Suppl.*] 8(19):103-107, 1973

5754 STUDY ON THE CORRELATION BETWEEN NORMOTEST, QUICK'S METHOD, AND SPECIFIC COAGULATION FACTORS IN LIVER DISEASE. *(E.)* Hadchouel, P.; Touboul, J. P.; Caroli, J. (St.-Antoine Hosp., Paris, France). *Scand. J. Gastroenterol.* [*Suppl.*] 8(19):151-154, 1973.

5755 NORMOTEST IN ACUTE VIRAL HEPATITIS. *(E.)* Schmidt, W.; Gros, H. (City Hosp., Saarbrucken, Germany). *Scand. J. Gastroenterol.* [*Suppl.*] 8(19):143-150, 1973.

5756 STATISTICAL EVALUATION OF NORMOTEST IN A LONGITUDINAL STUDY OF HEPATITIS. *(E.)* Hentschel, E.; Dittrich, H.; Havelec, L. (Hanusch Hosp., Vienna, Austria). *Scand. J. Gastroenterol.* [*Suppl.*] 8(19):139-141, 1973.

5757 PERCUTANEOUS LIVER BIOPSY. A REVIEW OF 200 CASES. *(E.)* Reid, N. C. R. W.; Schuster, M. M. (no affil.). *Md. State Med. J.* 22(5):43-46, 1973.

5758 STATISTICAL CORRELATIONS BETWEEN THE VALUES OF SOME LIVER FUNCTION TESTS AND THE EXTENT OF HEPATOCELLULAR INSUFFICIENCY. *(It.)* Proto, C.; Grasso, G.; Negretti, G.; Levi, G.; Spandrio, L.; Albertini, A.; Rossi, O. (Munic. Hosp., Brescia, Italy). *Fegato* 18(1):49-56, 1972.

5759 STATISTICAL ANALYSIS OF THE RELATIONSHIP BETWEEN SERUM CHOLINESTERASE AND OTHER LIVER FUNCTION TESTS. *(It.)* Proto, C.; Grasso, G.; Negretti, G.; Levi, G.; Spandrio, L.; Albertini, A.; Rossi, O. (Munic. Hosp., Brescia, Italy). *Fegato* 18(1):43-47, 1972.

5760 PERCUTANEOUS TRANSHEPATIC CHOLANGIOGRAPHY. *(E.)* Olbert, F.; Gaudernak, T.; Miess, F. (Lainz Hosp., Vienna, Austria). *Radiol. Clin. Biol.* 41(6):453-465, 1972.

5761 LAPAROSCOPY OR PERCUTANEOUS LIVER BIOPSY? *(E.)* Gros, H. (no affil.). *Munch. Med. Wochenschr.* 115(12):492-494, 1973.

5762 DETECTION OF ANTIBODY TO HEPATITIS-ASSOCIATED ANTIGEN BY INDIRECT COUNTER-IMMUNO-ELECTROPHORESIS. *(E.)* Tripodi, D.; Hawk, J.; Gocke, D. J.; Redeker, A.; Starkovsky, N. A. (Ortho Res. Fdn., Raritan, N.J.). *Am. J. Clin. Pathol.* 59:549-551, 1973.

5763 DETECTION OF VIRUS ANTIGENS: HEPATITIS B ANTIGEN. *(E.)* Walsh, J. H. (VA Wadsworth Hosp. Ctr., Los Angeles, Calif.). *Metabolism* 22(8):1111-1118, 1973.

5764 AN EVALUATION OF THE HOLLANDER TEST BY GRADED VAGOTOMY IN THE DOG. *(E.)* Nundy, S.; Baron, J. H. (Roy. Postgrad Med. Sch., London, England). *Gut* 14(8):665-668, 1973.

5765 INDICATIONS AND RESULTS OF LIVER NEEDLE BIOPSY IN CHILDHOOD. *(Ger.)* Feist, D.; Rossner, J. A.; Stefan, H. (Child. Clin., Univ. Heidelberg, Germany). *Monatsschr. Kinderheilkd.* 120(12):491-498, 1972.

5766 INTRAUTERINE DIAGNOSIS OF FETAL LIVER DYSFUNCTION. *(E.)* Beecham, J. B.; Braun, Jr., T. E.; Clapp, III, J. F.; Lucey, J. F. (Dept. Pediatr., Univ. Vermont, Burlington). *Obstet. Gynecol.* 41(4):556-562, 1973.

5767 COLONOSCOPY IN ULCERATIVE COLITIS. *(E.)* Shearman, J. C. (Roy. Infirm., Edinburgh, Scotland). *Scand. J. Gastroenterol.* 31(3):289-291, 1973.

5768 THE TECHNICAL APPROACH TO THE ACUTE ABDOMEN. *(E.)* Miller, R. E. (Indiana Univ. Sch. Med., Indianapolis). *Semin. Roentgenol.* 8(3):267-279, 1973.

5769 DIAGNOSTIC VALUE OF THE ESTIMATION OF GLUCOSE IN ASCITIC FLUID. *(E.)* Polak, M.; Torres da Costa, A. C. (Med. Fac., Univ. Sao Paulo Brazil). *Digestion* 8(4):347-352, 1973.

5770 COLOSCOPY, THE NEGLECTED PROCEDURE. *(E.)* Jackson, B. R. (St. Vincent's Hosp., Los Angeles, Calif.). *Dis. Colon Rectum* 16(4):278-282, 1973.

5771 GASTROPHOTOGRAPHY-GASTROSCOPY. AN EXPERIMENTAL STUDY. *(E.)* Fruhmorgen, P.; Demling, L.; Seiler, C. F.; Classen, M. (Dept. Med., Univ. Erlangen-Nuremberg, Germany). *Endoscopy* 4(3):133-141, 1972.

5772 ENDOSCOPY OF THE WHOLE INTESTINE. PRELIMINARY COMMUNICATION. *(E.)* Deyhle, P.; Jenny, S.; Fumagalli, J.; Linder, E.; Ammann, R. (Dept. Med., Univ. Zurich, Switzerland). *Endoscopy* 4(3):155-157, 1972.

5773 ENDOSCOPIC-BIOPTICAL DIAGNOSIS OF ANTRAL MUCOSA WITHIN THE DUODENAL STUMP. *(E.)* Pohl, W.; Flachsenberg, E.; Elster, K. (Munic. Hosp., Bayreuth, Germany). *Endoscopy* 4(3):162-163, 1972.

5774 PANVIEW FIBERSCOPIC EXAMINATION IN MARKED KYPHOSIS. *(E.)* Yamada, K.; Maruyama, M.; Koung-Dou, C.; Takemoto, T. (Tokyo Women's Med. Coll., Japan). *Endoscopy* 4(4):232-234, 1972.

5775 FIBERCOLONOSCOPY. *(E.)* Latts, J. R.; Borken, S. H.; Kaplan, A. (VA Hosp., Los Angeles, Calif.). *Minn. Med.* 56(8):665-667, 1973.

5776 THE PARASITOLOGIC DIAGNOSIS OF STRONGYLOIDIASIS IN THE STOOLS. *(Fr.)* Siffert, Jr., G. (Gen. Polyclin., Rio de Janeiro, Brazil). *Acta Gastroenterol. Belg.* 35(10-11):499-506, 1972.

5777 ABSENCE OF AN AGE EFFECT ON SULFOBROMOPHTHALEIN RETENTION IN HEALTHY MEN. *(E.)* Koff, R. S.; Garvey, A. J.; Burney, S. W.; Bell, B. (Boston VA Hosp., Massachussetts). *Gastroenterology* 65(2):300-302, 1973.

5778 CYTOLOGY IN GASTROENTEROLOGICAL DIAGNOSIS. *(E.)* Weidenhiller, S. (Dept. Intern. Med., Univ. Erlangen-Nurnberg, Germany). *Acta Hepatogastroenterol.* 19(6):469-476, 1972.

5779 THE PRECANCEROUS STATE OF THE STOMACH. *(E.)* Elster, K. (Munic. Hosp., Bayreuth, Germany). *Acta Hepatogastroenterol.* 20(1):49-51, 1973.

5780 CONGENITAL MALFORMATION OF THE PYLORUS (X-RAY FINDINGS OF A PYLORIC BAND). *(E.)* Fuchs, H.; Soballa, G.; Fruhmorgen, P. (Dept. Med., Univ. Erlangen-Nurnberg, Germany). *Acta Hepatogastroenterol.* 20(1):82-85, 1973.

5781 A SIMPLE ULTRAMICROMETHOD FOR INDIRECT SERUM BILIRUBIN DETERMINATION. *(E.)* Jezerniczky, J. (Univ. Med. Sch., Debrecen, Hungary). *Acta Paediatr. Acad. Sci. Hung.* 13(3):239-243, 1972.

5782 THE VALUE OF EMERGENCY ENDOSCOPY IN CAUSTIC ESOPHAGOGASTRITIS. *(E.)* Borjas, J. A. O.; Quiros, E. (Gen. Hosp. Social Security, Caracas, Venezuela). *Am. J. Gastroenterol.* 60(1):70-73, 1973.

5783 ARTERIOGRAPHY IN DIAGNOSIS OF ACUTE GASTROINTESTINAL TRACT BLEEDING. *(E.)* Stanley, R. J.; Wise, L. (Mallinckrodt Inst. Radiol., St. Louis Mo.). *Arch. Surg.* 107(2):138-144, 1973.

5784 IS THE XYLOSE TEST STILL A WORTH-WHILE INVESTIGATION? *(E.)* Sladen, G. E.; Kumar, P. J. (St. Bartholomew's Hosp., London, England). *Br. Med. J.* 3(5873):223-226, 1973.

5785 STUDIES ON THE DETERMINATION OF LIPASE ACTIVITY. *(E.)* Verduin, P. A.; Punt, J. M. H. M.; Kreutzer, H. H. (Lab. R. K. Ziekenverpleging, Hilversum, Netherlands). *Clin. Chim. Acta* 46(1):11-19, 1973.

5786 DEMONSTRATION OF AUSTRALIA ANTIGEN IN THE LIVER BY IMMUNOFLUORESCENCE. *(Ger.)* Muller, R.; Maess, J.; Deicher, H. (Hannover Med. Coll., Germany). *Dtsch. Med. Wochenschr.* 98(3):93-99, 1973.

5787 NORMAL FAECAL BLOOD LOSS AFTER INJECTION OF ^{51}Cr-LABELLED RED CELLS. *(E.)* O'Neill, B. J.; Shum, H. Y.; Streeter, A. M. (Repatriation Gen. Hosp., Concord, Australia). *Lancet* (7823):262, 1973.

5788 ANGIOGRAPHIC TECHNICS IN ASSESSING THE PATENCY OF PORTACAVAL ANASTOMOSES. *(E.)* Conn, H. O.; Ramsby, G. R. (VA Hosp., West Haven, Conn.). *Am. J. Dig. Dis.* 18(8):651-660, 1973.

5789 PLASMA AND URINE RIBONUCLEASE AS A MEASURE OF NUTRITIONAL STATUS IN CHILDREN. *(E.)* Sigulem, D. M.; Brasel, J. A.; Velasco, E. G.; Rosso, P.; Winick, M. (Cornell Univ. Med. Coll., New York, N.Y.). *Am. J. Clin. Nutr.* 26(8):793-797, 1973.

5790 LIVER SCINTIPHOTOGRAPHY AS AN INDEX OF LIVER ABNORMALITY. *(E.)* Mangum, J. F.; Powell, M. R. (Martinez VA Hosp., Calif.). *J. Nucl. Med.* 14(7):484-489, 1973.

5791 ENDOSCOPIC DIAGNOSIS OF A CONGENITAL INCOMPLETE DIAPHRAGMATIC OBSTRUCTION OF THE DUODENUM. *(E.)* Peters, H. (Surg. Dept. Med. Fac., RWTH, Aachen, Germany). *Endoscopy* 4(3):167-169, 1972.

5792 GASTROPHOTOGRAPHY OF THE UPPER PART OF THE STOMACH. *(E.)* Chang, F. M.; Chi, P. H.; Saito, T.; Ashizawa, S. (Tokyo Med. Coll. Hosp., Japan). *Endoscopy* 4(3):125-133, 1972.

5793 FIBERCOLONOSCOPY WITHOUT THE HELP OF FLUOROSCOPY. *(E.)* Nagasako, K.; Takemoto, T. (Tokyo Women's Med. Coll., Japan). *Endoscopy* 4(4):208-212, 1972.

5794 IMPROVED SENSITIVITY OF THE ELECTROPHORESIS METHOD BY TANNIC ACID FOR DETECTION OF AUSTRALIA ANTIGEN. *(E.)* Hopkins, R.; Das, P. C. (Roy. Infirm., Edinburgh, Scotland). *J. Clin. Pathol.* 25(9):832-833, 1972.

5795 INTRAVENOUS RADIONUCLIDE HEPATOGRAPHY IN THE DIFFERENTIAL DIAGNOSIS OF INTRAHEPATIC MASS LESIONS. *(E.)* Yeh, S. H.; Shih, W. J.; Liang, J. C. (Veterans Gen. Hosp., Taipei, Taiwan). *J. Nucl. Med.* 14(8):565-567, 1973.

5796 THE ACUTE ABDOMEN IN THE PEDIATRIC AGE GROUP. *(E.)* Singleton, E. B.; Wagner, M. L. (St. Luke's Episcopal Hosp., Houston, Texas). *Semin. Roentgenol.* 8(3):339-356, 1973.

5797 PROGRESS IN BRONCHOESOPHAGEAL ENDOSCOPY. *(E.)* Rosenow, III., E. C.; Hughes, Jr., R. W. (no affil.). *Surg. Clin. North Am.* 53(4): 775-783, 1973.

5798 PREOPERATIVE ASSESSMENT FOR HEPATIC METASTASES IN CARCINOMA OF THE COLON AND RECTUM. *(E.)* Ranson, J. H. C.; Adams, P. X.; Logalio, S. A. (New York Univ. Med. Sch., New York). *Surg. Gynecol. Obstet.* 137(3):435-438, 1973.

5799 EVALUATION OF A LATEX AGGLUTINATION TEST FOR AMOEBIASIS. *(E.)* Stamm, W. P.; Ashley, M. J.; Parelkar, S. N. (Roy. Free Hosp., London, England). *Trans. R. Soc. Trop. Med. Hyg.* 67(2):211-214, 1973.

5800 DIAGNOSIS OF THE "RESIDUAL GALLBLADDER." *(Rus.)* Pekerman, M. Ya.; Petrov, A. F. (Belgorod Region. Hosp., USSR). *Vestn. Khir. Grekov.* 103(1):34-37, 1972.

5801 THE APPLICATION OF A SPECIAL DEVICE FOR CYTOLOGIC DIAGNOSIS OF ESOPHAGEAL CANCER. *(Rus.)* Monakhov, B. V.; Shibanova, A. I.; Abdrakhmanov, Z. N. (Kazakh Res. Inst. Oncol. Radiol., Alma-Ata, USSR). *Vopr. Onkol.* 19(3):38-43, 1973.

See also, 5809, 5923, 5955, 5957, 5975, 6033.

GASTROINTESTINAL DISEASES

ESOPHAGUS

5802 ESOPHAGEAL PERFORATIONS AND FISTULAS: REVIEW OF 36 CASES WITH OPERATIVE CLOSURE OF FOUR CHRONIC FISTULAS. *(E.)* Hardy, J. D.; Tompkins, W. C.; Ching, E. C.; Chavez, C. M. (Univ. Mississippi Med. Ctr., Jackson). *Ann. Surg.* 177(6):788-797, 1973.

A review was made of 36 patients who had esophageal perforation or nonneoplastic chronic fistulas. Instrumentation accounted for 16 perforations, external trauma 6, Boerhaave's postemetic rupture 7, spontaneous benign fistulas 5, and foreign body 2. Patients who had sustained acute esophageal perforation almost invariably had pain and usually exhibited fever and leukocytosis. Plain posteroanterior and lateral neck and chest films were often helpful, but definitive diagnosis with demonstration of the site of perforation was usually achieved by esophagogram with water-soluble contrast medium. Treatment ranged from noninvasive management in minor perforation of the cervical esophagus, to formal thoracotomy and suture closure of perforation of the thoracic esophagus. There were 3 deaths in 16 patients who sustained instrumental perforation. Four patients with chronic fistulas, 3 with esophago-respiratory, and 1 with esophago-cutaneous fistula were operated upon and the defect closed. Of these 4, 2 were children with recurrent congenital tracheoesophageal fistulas that had been closed at birth. Of 7 patients with spontaneous rupture of the esophagus, 3 underwent operative closure and survived. Before operation could be performed 2 died. The remaining 2, 1 of whom was an infant, survived; 2 patients died prior to operation. The remaining 2, 1 of whom was an infant, survived without operative closure. The hazards of esophagogastric endoscopy are real. The new fiberoptic instruments, increased experience on the part of the operator, prompt diagnosis of the injury, appropriate surgical treatment, and vigorous supportive management will reduce the incidence and mortality rates due to esophageal perforation.

5803 CLINICAL ANALYSIS OF REFLUX ESOPHAGITIS IN SYMPTOMATIC PATIENTS. *(E.)* Akdamar, K.; Maumus, L. T.; Ichinose, H.; Font, R. G.; Sparks, R. D. (Tulane Univ. Sch. Med., New Orleans, La.). *Gastrointest. Endosc.* 19(4):172-173, 1973.

Reflux esophagitis was studied in 40 patients (34 females and 6 males, aged 31-76 yr). A modified Bernstein test was performed in which 0.9% NaCl solution was dripped at 120 drops/min for 5 min through a nasogastric tube. If no symptoms developed, the solution was changed to 0.1 N HCl. About 48 hr after the acid drip test, an esophagoscopic examination was performed. Patients who had symptoms and a positive acid-drip test had the following esophagoscopic results: severe mucosal hyperemia (9 patients), erosions and ulcers (9), stricture formation (3), atrophic esophageal mucosa (18), and hiatal hernia (24). In 14 patients, 24 specimens were obtained by pinch biopsies, of which only 3 were adequate. In 26 patients, 46 suction biopsy specimens were obtained, of which 39 were adequate. The low yield (12%) of adequate pinch biopsies compared to 78% adequate yield of suction biopsies was apparently due to the traumatic effect of the former procedure. Fragmentation, stripping, and tangential sectioning occurred in the majority of the defective pinch specimens. When erosions and ulcerations are seen at endoscopy, the diagnosis of esophagitis is obvious, and both forceps and suction biopsy methods will show inflammatory changes. Unfortunately, in most cases, the mucosal change is limited to atrophy. If the endoscopist fails to recognize this change he may not consider the diagnosis of esophagitis or obtain a mucosal biopsy.

5804 KINETICS OF FAT INHIBITION OF THE LOWER ESOPHAGEAL SPHINCTER. *(E.)* Nebel, O. T.; Castell, D. O. (U.S. Naval Hosp., Philadelphia, Pa.). *J. Appl. Physiol.* 35(1):6-8, 1973.

The relation of a fat meal effect to the known stimulatory effect of pentagastrin on esophageal sphincter pressure was investigated. A dose response curve for the lower esophageal sphincter response to i.v. pentagastrin in fasting subjects was sigmoid in shape with a peak change in lower esophageal spincter pressure of 38.0 mm Hg at 0.6 µg/kg. After ingestion of a fat meal, the pentagastrin dose response curve showed a parallel shift to the right. A pentagastrin dose of 1.0 µg/kg was required to produce a sphincter pressure change (34.2 mm Hg) which was not significantly different from the peak response obtained in the fasting state. These studies indicate that fat-induced inhibition of the lower esophageal sphincter most likely acts, at least partially, through antagonism of gastrin; and that the mechanism of this gastrin antagonism would appear to be one of competitive inhibition.

5805 PARAESOPHAGEAL HIATAL HERNIA: ENDOSCOPIC FINDINGS. REPORT OF A CASE. *(E.)* Bruni, H.; Lilly, J.; McHardy, G. (Louisiana State Univ. Sch. Med., New Orleans). *Am. J. Gastroenterol.* 57(6):563-565, 1972.

Endoscopic criteria for the diagnosis of sliding hiatal hernia were documented previously. A large paraesophageal hiatal hernia, well defined radiologically, is now documented by gastroscopy, performed on a 61 yr old female. The paraesophageal displacement of the gastric fundus through the wide diaphragmatic defect was accompanied by a segment of transverse colon. An associated upward displacement of the gastroesophageal junction was also identified by esophagoscopy and esophageal motility study. The diagnosis of paraesophageal hiatal hernia is made primarily by roentgenography. On operation it was determined that there was a 6 cm defect in the esophageal hiatus of the diaphragm with herniation of the stomach, duodenum, and transverse colon through the defect. Gastroscopic examination with the Olympus GTFA gastrocamera proved valuable in this case, permitting direct visualization of the involved segment of the stomach, and depiction of the herniation's paraesophageal orientation.

5806 PATHOGENESIS OF LOWER-ESOPHAGEAL-SPHINCTER INCOMPETENCE. *(E.)* Lipshutz, W. H.; Gaskins, R. D.; Lukash, W. M.; Sode, J. (Natl. Naval Med. Ctr., Bethesda, Md.). *N. Engl. J. Med.* 289(4):182-184, 1973.

The pathogenesis of diminished lower esophageal sphincter pressure has been studied in patients with symptomatic gastroesophageal reflux. In 23 patients, the lower esophageal-sphincter response to direct muscle stimulation by a parasympathomimetic drug (bethanechol chloride, 40 µg/kg) and to the effect of a cholinesterase inhibitor (edrophonium chloride, 80 µg/kg) was identical to that in 20 controls. Complete dose-response curves of lower esophageal sphincter pressure to exogenous pentagastrin (0.025-0.6 µg/kg, i.v.) were also similar in both groups. The response to endogenous gastrin release was diminished in patients with reflux. Pressure increased in response to gastric deacidification in reflux subjects by 1.5 mm Hg (70.5%) and by 10.5 mm Hg (197.5%) in the controls. The response to the gastric infusion of glycine was 2.3 mm Hg (35.7%) in patients with reflux as compared to 19.4 mm Hg (118.4%) in control subjects. It is suggested that a diminished release of endogenous gastrin may be responsible for decreased sphincter pressure in patients with gastroesophageal reflux.

5807 ESOPHAGEAL MOTILITY STUDIES. *(E.)* Nagler, R. W.; Rosof, B. M.; Katzka, I. (North Shore Hosp., Huntington, N.Y.). *N.Y. State J. Med.* 73(9):1073-1077, 1973.

5808 GASTRIC FUNDOPLICATIONS IN ESOPHAGEAL SURGERY OTHER THAN HIATIAL HERNIA REPAIRS. A REVIEW OF EXPERIMENTAL STUDIES AND CLINICAL APPLICATIONS. *(E.)* Butterfield, W. C. (Univ. Connecticut Sch. Med., Hartford). *Rev. Surg.* 30(2):77-83, 1973.

5809 INSIDE TRACHEOESOPHAGEAL FISTULA: NEW ENDOSCOPIC APPROACHES. *(E.)* Gans, S. L.; Berci, G. (Cedars-Sinai Med. Ctr., Los Angeles, Calif.). *J. Pediatr. Surg.* 8(2):205-211, 1973.

5810 THE RADIOLOGY CORNER. ESOPHAGEAL MONILIASIS. *(E.)* Siegel, H. A. (Sch. Med. Univ. California, San Diego). *Am. J. Gastroenterol.* 59(5):454-457, 1973.

5811 FIBERENDOSCOPIC FOREIGN BODY REMOVAL FROM THE UPPER GASTROINTESTINAL TRACT. *(E.)* Rosch, W.; Classen, M. (Dept. Med., Univ. Erlangen-Nuremberg, Germany). *Endoscopy* 4(4):193-197, 1972.

5812 ACHALASIA IN MOTHER AND DAUGHTER. *(E.)* Kilpatrick, Z. M.; Milles, S. S. (Med. Coll. Georgia, Augusta). *Gastroenterology* 62(5): 1042-1046, 1972.

5813 VALUE OF AZYGOGRAPHY IN PATIENTS WITH CARCINOMA OF THE ESOPHAGUS. *(E.)* Yamasaki, M.; Yamamoto, M.; Sato, M.; Sakai, K. (Niigata Univ. Sch. Med., Japan). *Acta Med. Biol.* 20(1):11-18, 1972.

5814 RADIOTHERAPY FOR ESOPHAGEAL CARCINOMA WITH DISTANT LYMPH NODE METASTASIS. REPORT OF A CASE SURVIVING OVER SIX YEARS AFTER TREATMENT. *(E.)* Sakai, K.; Sato, T. (Niigata Univ. Sch. Med., Japan). *Acta Med. Biol.* 20(1):19-25, 1972.

5815 A CASE OF SYNCOPE ON SWALLOWING SECONDARY TO OESOPHAGEAL SPASM. *(E.)* Alstrup, P.; Pedersen, S. A. (Odense Univ. Hosp., Denmark). *Acta Med. Scand.* 193(4):365-368, 1973.

5816 LYMPHANGIOMA OF THE ESOPHAGUS - DIAGNOSIS BY ENDOSCOPIC BIOPSY. *(E.)* Brady, P. G.; Milligan, F. D. (Johns Hopkins Hosp., Baltimore, Md.). *Am. J. Dig. Dis.* 18(5):423-425, 1973.

5817 CELESTIN-TUBE PALLIATION FOR MALIGNANT ESOPHAGEAL OBSTRUCTION. *(E.)* Sanfelippo, P. M.; Bernatz, P. E. (no affil.). *Surg. Clin. North Am.* 53(4):921-926, 1973.

5818 THE PRESENT STATE OF ONE-STAGE PHARYNGO-ESOPHAGEAL DIVERTICULECTOMY. *(E.)* Welsh, G. F.; Payne, W. S. (no affil.). *Surg. Clin. North Am.* 53(4):953-958, 1973.

5819 ESOPHAGEAL GRAFT PROTECTION WITH INTACT OMENTUM. *(E.)* Goldsmith, H. S.; Alday, E. S.; Mikoshiba, Y. (Jefferson Med. Coll., Philadelphia, Pa.). *Surg. Gynecol. Obstet.* 137(2):231-234, 1973.

5820 ROLE OF RADIATION THERAPY IN ESOPHAGEAL CARCINOMA. *(E.)* Ochsner, S. F.; Collins, V. P. (Ochsner Clin., New Orleans, La.). *South. Med. J.* 65(10):1165-1170, 1972.

5821 DYSPHAGIA IN CHILDHOOD. *(E.)* Myers, N. A. (Roy. Children's Hosp., Melbourne, Australia). *Aust. N.Z. J. Surg.* 42(4):365-368, 1973.

See also, 5782, 5797, 5801.

STOMACH

5822 A COMPARISON OF GASTRIC ACID BACK-DIFFUSION IN CONTROL AND ALCOHOLIC PATIENTS. *(E.)* Schneider, R. P.; Bernstein, R. B. (Boston City Hosp., Mass.) *Am. J. Dig. Dis.* 18(7):567-572, 1973.

To test gastric mucosal integrity, acid infusion studies were conducted on ten chronic male alcoholics, 28-65 yr old, admitted after recent heavy ethanol intake. The results were compared to a group of control patients. In addition, gastroscopic examinations were done on 11 of the alcoholic patients. It was found that 24 to 72 hr after ethanol ingestion, the response of the mucosal barrier to acid instillation in chronic alcoholics was similar to that in the control group. There was no evidence of increased back-diffusion. Gastroscopy revealed only minor mucosal changes in 4 of the 10 patients. Further studies are necessary to explain the relation between alcohol, back diffusion of acid and erosive gastritis.

5823 GASTRIC MUCOSAL MORPHOLOGY AND FAECAL BLOOD LOSS DURING ETHANOL INGESTION. *(E.)* Dinoso, Jr., V. P.; Meshkinpour, H.; Lorber, S. H. (Temple Univ. Sch. Med., Philadelphia, Pa.). *Gut* 14(4):289-292, 1973.

The fecal blood loss of 6 alcoholic subjects with normal gastric mucosa, 6 with superficial gastritis, and 6 with atrophic gastritis was studied before and during ingestion of 40% v/v ethanol using ^{51}Cr-tagged red blood cells. Abnormalities in platelet count, prothrombin time, partial thromboplastin time, and bleeding time were not observed before or after ethanol administration. No significant change in fecal blood loss was observed in the normal mucosa and superficial gastritis groups, but all subjects with atrophic gastritis had significant increases of fecal blood loss during ethanol ingestion. These observations suggest that gastric mucosal morphology may be an important determinant of gastric mucosal bleeding during the ingestion of alcohol. The inherent thinness and increased tendency of the epithelial lining cells to exfoliate in a mucosa with atrophic gastritis could contribute to the increased loss of red blood cells during the basal state as well as to the development of mucosal erosions and bleeding on exposure to ethanol.

5824 HYPERGASTRINAEMIA IN RHEUMATOID ARTHRITIS: DISEASE OR IATROGENESIS. *(E.)* Rooney, P. J.; Vince, J.; Kennedy, A. C.; Webb, J.; Lee, P.; Dick, W. C.; Buchanan, K. D.; Hayes, J. R.; Ardill, J.; O'Connor, F. (Roy. Infirm., Glasgow, Scotland). *Br. Med. J.* 2(5869):752-753, 1973.

Fifty patients with classical or definite rheumatoid arthritis were studied (35 females and 15 males, mean age 54.4 yr). The mean fasting plasma gastrin level of 171 ± 38 pg/ml was significantly greater than the level in control subjects of 56 ± 8 pg/ml. In 8 patients with rheumatoid arthritis, the plasma gastrin level was greater than 1000 pg/ml. In 5 patients, gastric parietal cell antibodies were found. Of these 5, 1 had a normal gastrin level and only 2 had levels greater than 1000 pg/ml. Thus, chronic atrophic gastritis seems unlikely as a cause of hypergastrinemia. No obvious relation was found between gastrin levels and the severity of the arthritis. No particular drug emerged as a likely etiological agent; the possibility that this is a property of the anti-inflammatory drugs as a group is under review. It is noted that of 7 patients who complained of dyspepsia, only 1 had a raised gastrin level.

5825 EFFECT OF PROXIMAL GASTRIC VAGOTOMY ON GASTRIC ACID SECRETION AND PLASMA GASTRIN. *(E.)* Clark, C. G.; Lewin, M. R.; Stagg, B. H.; Wyllie, J. H. (Univ. Coll. Hosp. Med. Sch., London, England). *Gut* 14(4):293-299, 1973.

Proximal gastric vagotomy (highly selective vagotomy) for chronic duodenal ulceration was performed on 16 patients, 13 males and 3 females. All were subjected to preoperative and postoperative acid secretion studies. Before operation the mean basal acid secretion was 3.96 mEq/hr which increased to 19.31 mEq/hr after meat extract and 38.75 mEq/hr after 6 μg/kg s.c. pentagastrin. A reduction in the secretory response to pentagastrin and abolition of the response to meat extract occurred postoperatively. Plasma gastrin levels in response to meat extract were studied by radioimmunoassay. Basal plasma gastrin levels were unaffected by vagotomy. Before operation the mean plasma gastrin level was 92 pg/ml under fasting conditions and 250 pg/ml after meat extract. In 8 patients with negative postoperative insulin tests, operation reduced the mean plasma gastrin response to meat extract to 135 pg/ml. This response was not impaired postoperatively in the 8 insulin-positive patients.

326 THE INCIDENCE OF GASTRIC AND THYROID AUTOIMMUNITY IN INSULIN-DEPENDENT GREEK DIABETIC ATIENTS. *(E.)* Kanaghinis, T.; Fostiropoulos, G.; atsou, P.; Ikkos, D.; Karayannis, S.; Kouris, C.; ardikas, C. (Evangelismos Hosp., Athens, Greece). *n. J. Dig. Dis.* 18(2):92-98, 1973.

827 INFARCTION OF THE STOMACH FOLLOWING ATHEROMATOUS EMBOLIZATION: REPORT OF A CASE AND ITERATURE REVIEW. *(E.)* Harvey, R. L.; Doberneck, . C.; Black, III, W. C. (Univ. New Mexico Sch. Med., lbuquerque). *Gastroenterology* 62(3):469-472, 1972.

328 GASTROSCOPIC REMOVAL OF A PHYTOBEZOAR. *(E.)* McKechnie, J. C. (Methodist Hosp., uston, Texas). *Gastroenterology* 62(5):1047-1051, 72.

329 SPONTANEOUS IDIOPATHIC RUPTURE OF THE STOMACH IN THE NEONATAL PERIOD. *(E.)* nes, J.; Lukacs, F. V.; Leb, J. (Apathy Children's sp., Budapest, Hungary). *Acta Paediatr. Acad. Sci. ng.* 13(3):253-258, 1972.

30 ADULT HYPERTROPHIC PYLORIC STENOSIS. *(E.)* MacDonald, J. A. (Western Infirm., Glasgow, otland). *Br. J. Surg.* 60(1):73-75, 1973.

31 DUPLICATION OF THE PYLORUS (GASTRODUODENAL BAND). *(E.)* Fruhmorgen, P.; Koniszewski, ; Classen, M. (Dept. Med., Univ. Erlangen-Nuremberg, rmany). *Endoscopy* 4:234-237, 1972.

32 LYMPHORETICULAR HYPERPLASIA OF THE STOMACH (PSEUDOLYMPHOMA). *(E.)* Nelson, R. S.; nza, F. L.; Bottiglieri, N. G. (Dept. Med., Univ. x., Houston). *Gastrointest. Endosc.* 19(4):183-6, 1973.

33 METASTASES AND PRIMARY NEOPLASMS OF THE STOMACH IN PATIENTS WITH BREAST CANCER. *.)* Yoshida, Y. (Surg. Dept. Kyoto Univ., Japan). *. J. Surg.* 125(6):738-743, 1973.

34 ALPHA-FETOPROTEIN AND CARCINOEMBRYONIC ANTIGEN IN A CASE OF GASTRIC CARCINOMA TASTATIC TO THE LIVER. *(E.)* Bierfeld, J. L.; heiner, M. I.; Schultz, D. R.; Moral, M. D.; gers, A. I. (Univ. Miami Sch. Med., Fla.). *Am. J. g. Dis.* 18(5):517-520, 1973.

35 PRIMARY GASTRIC PLASMACYTOMA. CASE REPORT AND REVIEW OF THE LITERATURE. *(E.)* Godd, J. E.; Fox, J. E.; Levinson, M. J. (Naval Hosp., lando, Fla.). *Am. J. Dig. Dis.* 18(5):508-512, 73.

5836 GASTRIC CANCER. DIRECT VISION BIOPSY AND ABRASIVE CYTOLOGY. *(E.)* Gregg, J. A.; Garabedian, M.; Gibb, S. P.; Shah, A.; Shah, S.; Gokim, Jr., G. (Lahey Clin. Fdn., Boston, Mass.). *Am. J. Gastroenterol.* 59(5):401-409, 1973.

5837 "LIVING" WITZEL TUBE GASTROSTOMIES: AN EXPERIMENTAL STUDY OF PERMANENT VALVULAR GASTROSTOMIES USING JEJUNAL AND GASTRIC TUBES. *(E.)* Butterfield, W. C.; Massi, J. (McCook Hosp., Hartford, Conn.). *Am. Surg.* 39(6):355-357, 1973.

5838 CHRONIC OR RECURRING ORGANOAXIAL ROTATION OF THE STOMACH. *(E.)* Deitel, M. (St. Joseph's Hosp., Toronto, Ontario, Canada). *Can. J. Surg.* 16(3):195-205, 1973.

5839 AN EPIDEMIOLOGIC ANALYSIS OF MORTALITY AND GASTRIC CANCER IN NEWFOUNDLAND. *(E.)* Pfeiffer, C. J.; Fodor, J. G.; Canning, E. (Fac. Med., Mem. Univ. Newfoundland, Canada). *Can. Med. Assoc. J.* 108(11):1374-1380, 1973.

5840 GASTRIC CARCINOMA FOLLOWING LONG-TERM GASTROENTEROSTOMY. REPORT OF TWO CASES. *(E.)* Carter, T. L.; Martel, W. (Madison Gen. Hosp., Wisc.) *J.A.M.A.* 225(1):52-53, 1973.

5841 GASTRITIS AS A COMPLICATION OF VARICELLA. *(E.)* Baker, C. J.; Gilsdorf, J. R.; South, M. A.; Singleton, E. B. (Baylor Coll. Med., Houston, Tex.). *South. Med. J.* 66(5):539-541, 1973.

See also, 5575, 5764, 5771, 5779, 5782, 5792, 5808, 5811, 5846, 5871, 5872, 5886, 6116.

STOMACH

Peptic Ulcers

5842 INTRAGASTRIC PRESSURE, SECRETAGOGUE CHARACTERISTICS, AND PATHOGENESIS OF PHENYLBUTAZONE ULCER. *(E.)* Larmi, T. K.; Kairaluoma, M. I. (Dept. Surg., Univ. Oulu, Finland). *Scand. J. Gastroenterol.* 31(3):317-320, 1973.

Phenylbutazone (200 mg/kg, i.m.) reduced the volume of gastric secretion from 1.5 to 0.28 ml/100 g, intragastric pressure from 7.4 to 5.5 cm H_2O, and secretion of free hydrochloric acid from 40.2 to 2.9 mEq/liter in the rat, yet induced ulcers in the gastric corpus in about 50% of the experimental animals in 2 hr. Pyloric ligation did not increase the ulcer formation induced by phenylbutazone. When pyloric ligation and vagotomy were performed simultaneously on rats treated with phenylbutazone, gastric secretion fell to almost zero while intragastric pressure rose to 7.0 cm H_2O. Despite the increase in pressure, no ulcers developed. Hence a certain acidity of the gastric juice is necessary for ulcer formation. However, the hydrochloric acid secretion of the stomach was not the dominating factor in the pathogenesis of phenylbutazone-induced ulcer.

5843 A DOUBLE-BLIND STUDY OF THE EFFECT OF CARBENOXOLONE SODIUM IN THE TREATMENT OF GASTRIC ULCER. *(E.)* Geismar, P.; Mosbech, J.; Myren, J. (Copenhagen County Hosp., Copenhagen, Denmark). *Scand. J. Gastroenterol.* 8(3):251-256, 1973.

Of 34 patients with gastric ulcers, 18 were treated with 300 mg carbenoxolone daily for 1 week and thereafter with 150 mg daily for 3 weeks. The remaining patients were treated with placebo for the same periods. Gastroscopy and X-ray examination indicated a tendency to better ulcer healing in the carbenoxolone group, but the difference was not statistically significant. In the carbenoxolone group, there was a 3.5% weight gain, a decrease in serum potassium concentration, and a decrease in peak acid output; mean blood pressure increased by 20 mm Hg in 3 patients. During a 1-24 month observation period, about 40% of the healed ulcers recurred. Thus, short-term treatment with carbenoxolone does not protect against recurrence more than conventional conservative therapy.

5844 ACID RESPONSE TO PENTAGASTRIN IN RELATION TO AGE AND BODY STATURE IN MALE AND FEMALE ULCER PATIENTS. *(E.)* Borgstrom, S.; Emas, S.; Lilja, B.; Borg, I. (Dept. Surg., Univ. Lund, Malmo, Sweden). *Scand. J. Gastroenterol.* 8(3):209-216, 1973.

The peak acid output to pentagastrin, s.c., was determined in 154 male duodenal and 30 male corporal gastric ulcer patients, and in 50 female duodenal ulcer and 18 female corporal gastric ulcer patients. The response decreased significantly with age in male duodenal ulcers and corporal gastric ulcers patients independently of the response being expressed as peak acid output or as functions of body stature. In female patients the response tended to increase with age in duodenal ulcers and to decrease in corporal gastric ulcers. This was true for the peak acid output and peak acid output as functions of body stature. Both in males and females the response of the duodenal ulcers and corporal gastric ulcer patients did not differ in young patients but was higher in elderly patients with duodenal ulcer than corporal gastric ulcer. Since the acid response decreased with age in male duodenal ulcers and tended to increase in female duodenal ulcer patients, the acid response was higher in young and middle-aged male patients and equal or slightly higher in old female than male patients. The intercept between the regression lines (response versus age) for male and female duodenal ulcers was dependent on the response being expressed as peak acid output or as functions of body stature. In corporal gastric ulcer patients the peak acid output and the peak acid output related to body weight were higher in males than females, but the difference decreased with age. For comparison within the sexes, age was of major and body stature of minor importance; for comparison between the sexes, age and body stature were of major importance. It is evident from this study that comparisons of the acid response in ulcer patients without attention to age and sex might be hazardous.

5845 A TRIAL OF EXOGENOUS SECRETIN IN THE TREATMENT OF DUODENAL ULCER PAIN. *(E.)* Hoj, L.; Holst, J. J.; Rune, S. J. (Bispebjerg Hosp., Copenhagen, Denmark). *Scand. J. Gastroenterol.* 8(3):279-281, 1973.

In 15 patients (3 females and 12 males) with duodenal ulcer and 9 patients (3 females and 6 males) with X-ray negative dyspepsia, the effectiveness of pure natural secretin on upper epigastric pain (37.5 clinical U, s.c.) was tried in a doubleblind test against an injection of saline, applying a cross-over, random allocation design. Of 15 ulcer patients, 11 were relieved after secretin while 6 found saline effective. Of the 9 patients with dyspepsia without a demonstrable ulcer, 3 found relief after secretin and 2 after saline. Neither of these differences are statistically significant at the 5% level. Although a type 2 - or β error (i.e., failing to demonstrate an effect which actually does exist) is suspected, it must be concluded that exogenous secretin was not superior to saline in the treatment of duodenal ulcer pain.

5846 RELATIONSHIP BETWEEN VAGOTOMY, PEPTIC ULCER AND GASTRIC ADENOCARCINOMA IN RATS FED 2,7-DIACETYLAMINOFLUORENE. *(E.)* Kowalewski, K.

(Dept. Surg., Univ. Alberta, Edmonton, Canada). *Can. J. Surg.* 16(3):210-217, 1973.

Buffalo male rats were prepared for experimentation by bilateral vagotomy and/or by thermocautery induced gastric glandular ulcer. Carcinogen 2,7-diacetylaminofluorene was given orally in their daily diet (0.25 g of the carcinogen/kg dry diet). Control, carcinogen-fed rats had no operation. Operated rats were also kept on a normal diet and served as controls; they were not exposed to the carcinogen. Only rats exposed to 2,7-diacetylaminofluorene developed malignant gastric lesions. Gastric malignant tumors were classified as adenocarcinomas and mixed tumors (containing both glandular and epidermoid malignant cells). Gastric tumors were found in 6% of rats having no operation, in 25% of rats with peptic ulcer, in 18% of vagotomised animals and in 18% of rats having both surgical procedures. It was concluded that both vagotomy and the presence of injured gastric mucosa (ulcer) enhanced the malignant transformation of gastric glandular mucosa. Under the conditions of this experiment, vagotomy and the presence of peptic ulcer contributed to the development of gastric adenocarcinoma.

5847 EFFECT OF CARBENOXOLONE ON THE GASTRIC MUCOSAL BARRIER IN MAN AFTER ADMINISTRATION OF TAUROCHOLIC ACID. *(E.)* Ivey, K. J.; Gray, C. (Roy. Prince Alfred Hosp., Sydney, Australia). *Gastroenterology* 64(6):1101-1105, 1973.

The ability of carbenoxolone to prevent increased back diffusion of H^+ ions after intragastric instillation of a 10 mM solution of taurocholic acid was studied in 5 healthy human volunteers (4 males and 1 female, aged 21-23 yr). In control studies taurocholic acid produced a net loss of H^+ ions of -3.8 mEq/15 min and Na^+ gain of 3.6 mEq/15 min. With prior intragastric instillation of 100 mg of carbenoxolone, the net H^+ loss was -2.8 mEq/15 min and Na^+ gain was 3.1 mEq/15 min. These differences were not significant. Studies repeated in 3 subjects after a 3-week course of oral carbenoxolone showed similar results. It is concluded that the mechanism of action of carbenoxolone in healing gastric ulcers is unlikely to occur by preventing back diffusion of H^+ ions after bile reflux.

5848 ARTERIOMESENTERIC DUODENAL COMPRESSION SYNDROME. ITS ASSOCIATION WITH PEPTIC ULCER. *(E.)* Anderson, W. C.; Vivit, R.; Kirsh, I. E.; Greenlee, H.B. (VA Hosp., Hines, Ill.). *Am. J. Surg.* 125(6):681-689, 1973.

The diagnosis of arteriomesenteric duodenal compression syndrome is reviewed for 32 cases. Of the patients, 19 (59%) have associated peptic ulcer disease. Detection of the syndrome depends on a high index of suspicion, especially in patients with peptic ulcer or debilitating disease. It is suggested that radiologic studies are the key to diagnosis of this syndrome and the following criteria are presented: with radiology, visualization of intermittent obstruction to the passage of barium in the third portion of the duodenum; leading bolus of barium shows straight line cutoff at point of obstruction; dilatation of duodenum proximal to the obstruction; on cinefluorography, relief of obstruction in prone position, its accentuation in upright or supine position. Evidence suggests that the choice of treatment must be strictly individualized. When peptic ulcer surgery is contemplated, consideration must also be given to alleviation of the distal duodenal obstruction.

5849 SELECTIVE TRIPSIS OF THE VAGUS IN EXPERIMENTS AND THE THERAPY OF PEPTIC ULCER. *(E.)* Mlinaric, I. (Dr. M. Stojanovic Hosp., Zagreb, Yugoslavia). *Lijec. Vjesn.* 94(7):327-335, 1972.

5850 ULCERS OF THE GASTROINTESTINAL TRACT IN BURN DISEASE. *(Rus.)* Kaem, R. I. (A. V. Vishnevskii Inst. Surg., Moscow, USSR). *Arkh. Patol.* 34(10):36-42, 1972.

5851 PEPTIC ULCER IN VARANASI. *(E.)* Vaidya, M. P. (Inst. Med. Sci., Banaras Hindu Univ., Varanasi, India). *Q. J. Surg. Sci.* 8(2): 88-92, 1972.

5852 ON PATHOGENESIS OF PEPTIC ULCER OF THE STOMACH AND THE DUODENUM. *(Rus.)* Samsonov, V. A. (O. V. Kuusinen Univ., Petrozavodsk, USSR). *Arkh. Patol.* 34(10):3-11, 1972.

5853 PERFORATED GASTRIC ULCER IN A 4-YR-OLD CHILD. *(Dan.)* Rasmussen, P. (Hjorring Hosp., Denmark). *Ugeskr. Laeg.* 134(35):1852-1853, 1972.

5854 SUTURING OR PRIMARY RESECTION IN PERFORATED PEPTIC ULCER. *(Ger.)* Brunner, H.; Schmitt-Koppler, A. (Surg. Clin., Univ. Mainz, Germany). *Bruns Beitr. Klin. Chir.* 219(5):420-428, 1972.

5855 PERFORATING GASTRIC ULCERS WITH AN ATYPICAL CLINICAL PICTURE. *(Ser.)* Glitsic, Z.; Tasic, D.; Dugalic, D.; Djukic, V. (Med. Fac., Univ. Belgrade, Yugoslavia). *Srp. Ark. Celokup. Lek.* 100(2):185-192, 1972.

5856 HISTORY IN DUODENAL ULCER AND SCARRING. *(Ger.)* Fruhmorgen, P.; Jenny, S.; Classen, M.; Bauerle, H.; Koch, H. (Med. Clin., Univ. Erlangen-Nurnberg, Erlangen, Germany). *Dtsch. Med. Wochenschr.* 97(6):188-193, 1972.

5857 GASTRIC DRAINAGE IN THE FIRST DAYS AFTER VAGOTOMY. *(Cz.)* Langer, L. (Fac. Gen. Med., Charles Univ., Prague, Czechoslovakia). *Rozhl. Chir.* 51(8):529-534, 1972.

5858 NEW METHODS IN THE TREATMENT OF ULCERS. *(Ger.)* Blum, A. L. (Triemli Munic. Hosp., Zurich, Switzerland). *Schweiz. Med. Wochenschr.* 103(5):179-187, 1973.

5859 HYPOGLYCEMIC CONVULSIONS AFTER VAGOTOMY AND PYLOROPLASTY. *(E.)* Hall, W. H.; Sanders, L. L. (VA Hosp., Little Rock, Ark.). *South. Med. J.* 66(4):502-504, 1973.

5860 ACUTE PEPTIC ULCERS IN MEDICAL RESUSCITATION. *(Fr.)* Grivaux, M.; Alexandre, J. H.; Soulie, J.; Diallo, A.; Perles, C.; Chevalley, J. (Broussais Hosp., Paris, France). *Ann. Med. Interne (Paris)* 123(4):403-408, 1972.

5861 AFFERENT-EFFERENT LOOP INTRAGASTRIC INTUSSUSCEPTION: DIAGNOSED BY GASTROSCOPY. *(E.)* Woodward, J. C.; Mainz, D. L.; Webster, P. D. (Med. Coll. Georgia, Augusta). *Gastroenterology* 64(1): 120-122, 1973.

5962 GASTRIC ACID SECRETION BEFORE AND AFTER OPERATION IN THE PEPTIC ULCER PATIENTS. *(Jap.)* Konaka, K. (Konaka Hosp., Oita-ken, Japan). *J. Kumamoto Med. Soc.* 46(3):168-174, 1972.

5863 RADIOLOGICAL MANIFESTATIONS OF MARGINAL ULCER. *(E.)* Roosth, T. M.; Schreiber, M. H. (Univ. Texas Med. Br., Galveston). *Tex. Med.* 68(2):99-102, 1972.

5864 RETAINED GASTRIC ANTRUM. *(E.)* Beneventano, T. C.; Glotzer, P.; Messinger, N. H. (Montefiore Hosp., Bronx, N.Y.). *Am. J. Gastroenterol.* 59(4):361-365, 1973.

See also, 5721, 5736, 5737, 5773, 5774, 5825, 5891

SMALL INTESTINE

5865 SENSITIVITY AND SPECIFICITY IN TESTS OF DISTAL ILEAL FUNCTION: PROSPECTIVE COMPARISON OF BILE ACID AND VITAMIN B_{12} ABSORPTION IN ILEAL RESECTION PATIENTS. *(E.)* Fromm, H.; Thomas, P. J.; Hofmann, A. F. (Mayo Clin., Rochester, Minn.). *Gastroenterology* 64(6):1077-1090, 1973.

Bile acid and vitamin B_{12} absorption were compared prospectively in 22 patients with distal ileal resection, 7 with similar diarrhea but apparently normal ileal function, 5 with the stagnant loop syndrome, and 3 with steatorrhea due to digestive abnormalities. Also studied were 18 healthy control subjects. A 300-ml liquid test meal containing 10 μC glycine-^{14}C-labeled glycocholate, 10 μC ^{3}H-ring-labeled taurocholate, vitamin B_{12}-^{57}Co with intrinsic factor, and 2 μC $^{51}CrCl_3$ as nonabsorbable marker was administered to fasting patients. Bile acid absorption was assessed by appearance of $^{14}CO_2$ in breath and by fecal excretion of ^{14}C or ^{3}H; B_{12} absorption was measured by excretion of ^{57}Co in urine (Schilling test). Based on fecal excretion of ^{3}H, nearly all patients with ileal resection had unequivocal bile acid malabsorption. Measurement of $^{14}CO_2$ in breath was less sensitive and 4 false negatives were identified. Measurement of both $^{14}CO_2$ and fecal ^{14}C was as sensitive as measurement of fecal ^{3}H. Of the 14 patients with resections less than 100 cm, 4 had normal Schilling tests, despite nearly all having bile acid malabsorption; both tests were equivocal or abnormal in patients with larger resections. In patients with similar diarrhea but no evidence of ileal dysfunction, bile acid malabsorption was not present, since the ratio of fecal bile acid radioactivity to marker radioactivity was significantly smaller than in patients with ileal resection; B_{12} absorption was normal. The breath test appears to be a useful screening test for the detection of the stagnant loop syndrome. Its interpretation is uncertain in patients with ileal dysfunction, since such patients may also have bile acid malabsorption. Thus, the clinical value of the breath test for measurement of bile acid absorption in such patients probably can only be determined by future studies which relate test results to therapeutic response.

5866 THE ILEOCECAL SYNDROME IN ACUTE CHILDHOOD LEUKEMIA. *(E.)* Sherman, N. J.; Woolley, M. W.; (Children's Hosp., Los Angeles, Calif.). *Arch. Surg.* 107(1):39-42, 1973.

Secondary complications developed in the ileocecal region after drug-induced remission in 11 children (8 boys and 3 girls, aged 1 months to 9 yr) with acute leukemia. Six children had acute lymphocytic leukemia, 3 acute myelogenous leukemia, 1 congenital lymphocytic leukemia, and 1 acute erythroleukemia. The most commonly used chemotherapeutic agents were mercaptopurine and prednisone; the average time before onset of the complication was 8.8 months and from complication until death, 1.5 months. Presenting symptoms included abdominal pain (6), fever (4), distention (3), diarrhea (3), vomiting (2), right lower quadrant mass (1), sepsis (1), and hematemesis (1). Appendicitis was diagnosed in 5 and cecitis in 5; 1 patient had acute abdomen for which no cause could be found, even at surgery. Of the 5 with appendicitis, 2 had leukemia infiltrates and a local inflammatory reaction in the periappendiceal area; 2 others had gangrene which, in 1 case, was associated with generalized peritonitis; and 1 had an appendix which perforated into the distal ileum, resulting in an abscess. All of these children died of sepsis. Two of the 5 children with cecitis had sepsis; 1 underwent laparotomy and removal of a normal appendix and died 2 months later in relapse. The cecum perforated in 2 children, in one case forming a fistula with the sigmoid. No correlation was found between the ileocecal complication and any specific drug or combination of drugs.

5867 VILLOUS TUMORS OF THE DUODENUM AND JEJUNUM. REPORTS OF FOUR CASES AND REVIEW OF LITERATURE. *(E.)* Mir-Madjlessi, S.; Farmer, R. G.; Hawk, W. A. (Cleveland Clin. Fdn., Ohio). *Am. J. Dig. Dis* 18(5):467-476, 1973.

Patients with villous adenomas of the duodenum (2 females and 1 male, aged 46-72 yr) and of the jejunum (1 male aged 46 yr) have been studied. Symptoms and histories upon hospitalization were massive upper gastrointestinal bleeding with a history of alcohol consumption, several episodes of biliary colic and obstructive jaundice with a prior cholecystectomy for gallstone removal, vomiting and epigastric pain secondary to duodenal obstruction, and heartburn of 4 yr duration. Roentgenographic study of the upper gastrointestinal tract of these patients revealed esophageal and gastric varices, duodenal ulcer, hiatus hernia, and distortion of mucosal pattern with some narrowing of the lumen at the fourth portion of the duodenum. In each case the villous adenoma was revealed at laparotomy. In 3 of the 4 cases, microscopic examination of the lesion showed no evidence of malignancy. Treatment in these 3 cases included excision, Whipple's operation, and resection. In the 4th, microscopic examination showed adenocarcinoma arising from the villous tumor and invading the muscularis propria. Resection was performed. When no malignancy is evident, a limited resection or simple excision of the tumor is sufficient. However, in cases with malignancy, a more extensive resection is warranted.

5868 MECHANISM FOR HYPEROXALURIA IN PATIENTS WITH ILEAL DYSFUNCTION. *(E.)* Chadwick, V. S.; Modha, K.; Dowling, R. H. (Roy. Postgrad. Med. Sch., London, England). *N. Engl. J. Med.* 289(4):172-176, 1973.

Hyperoxaluria was found in 12 of 18 patients (aged 16 to 80 yr) who had undergone resection of the ileum for Crohn's disease (9), mesenteric vascular occlusion (6), tuberculosis (1), radiation ileitis (1), and postoperative ileal stricture (1). The present studies show that, in these patients, bile-salt glycine is not a precursor of urinary oxalate and glyoxylate metabolism is normal. However, patients with ileal resection and hyperoxaluria absorbed up to 5 times as much ^{14}C-oxalate as control subjects (mean of 31%, as compared with 6.6) when the isotope was given with food. Treatment of these patients with low oxalate diets (<4 mg of oxalate/24 hr) promptly abolished the hyperoxaluria. These results suggest that increased absorption of dietary oxalate is the cause of the hyperoxaluria seen in patients with ileal dysfunction.

5869 INTRALUMINAL PRECIPITATION OF BILE ACIDS IN STAGNANT LOOP SYNDROME. *(E.)* Northfield, T. C. (Guy's Hosp., London, England). *Br. Med. J.* 2(5869):743-745, 1973.

The postprandial concentrations of free and conjugated bile acids were measured in total content and micellar phase of jejunal aspirates from 9 patients with steatorrhea due to the stagnant loop syndrome and from 11 normal controls. All 9 patients had fecal fat excretion of more 5 g fat/day on a diet of about 75 g of fat/day. Small intestinal stricture was present in 4 subjects, small intestinal diverticula in 3, and fistulae between the small and large intestine in 2. Aspirates from patients with stagnant loop syndrome, but not from the normal controls, had a high concentration of free (unconjugated) bile acids. There was a reciprocal decrease in the concentration of conjugated bile acids, but total bile acid concentration in the whole aspirate remained normal. Total bile acid concentration in the micellar phase of intestinal content was reduced, indicating precipitation of bile acids. These findings suggest that precipitation of unconjugated bile acids, rather than passive absorption, leads to a reduced postprandial concentration of bile acids in the micellar phase of jejunal content, and are consistent with the hypothesis that fat malabsorption in the stagnant loop syndrome results from decreased micellar dispersion of lipolytic products.

5870 THE LABORATORY DIAGNOSIS OF INTESTINAL TUBERCULOSIS: A STUDY OF 50 CASES. *(E.)*

Singh, H. N.; Vaidya, M. P.; Roy, S. K. (Dept. Surg., Banaras Hindu Univ., Varanasi, India). *Aust. N.Z. J. Surg.* 42(4):411-415, 1973.

To rule out the possibility of regional enteritis, histopathological and bacteriological studies were performed on tissue from 50 patients with acute, subacute, or chronic intestinal obstruction and a suspected diagnosis of intestinal tuberculosis established by clinical, radiological, and surgical findings. At surgery lesions were found in the ileocecal region in 36 patients. The intestine was resected in 32 patients and bypass procedures were performed on 4 poor-risk patients. Lesions were hyperplastic in 24 cases and ulcerohyperplastic in 10; 14 patients had strictures of the small intestine, 1 had pseudopolyposis mimicking ulcerative colitis, and 1 had a submucous lipoma with chronic ileocolic intussusception. Lymph node biopsy gave unequivocal evidence of intestinal tuberculosis in 45 (90%) of these patients. Acid-fast bacilli were demonstrated in 4 of 25 cases (16%) by staining tissue from resected sections and lymph nodes with Ziehl-Neelsen stain, while culture of tissue homogenates in Lowenstein-Jensen media gave only 7 positive results in 48 cases (14.5%). The best bacteriological method for diagnosing intestinal tuberculosis consisted in inoculating guinea pigs i.p. or i.m. with tissue homogenates. Acid-fast bacilli were demonstrated directly by staining guinea pig tissues in 18 cases (47.3%). Granuloma formation occurred in 26 cases, with caseation in 23 of these 26.

5871 POSTOPERATIVE MOTILITY IN THE SMALL INTESTINE. *(E.)* Dahlgren, S.; Selking, O. (Univ. Hosp., Uppsala, Sweden). *Ups. J. Med. Sci.* 77(2):202-204, 1972.

The postoperative motility of the small intestine was studied by means of pressure-sensitive endoradiosondes in 13 patients who had undergone abdominal operations with and without enterotomy. Of the 13 patients, 5 had undergone cholecystectomy, 5 gastrectomy, 1 explorative laparotomy, 1 plastic repair of the diaphragmatic hernia and pyloroplasty, and 1 duodenopancreatectomy. Of the 5 gastrectomy patients, 4 underwent a Billroth I and 1 a Billroth II resection, and in 1 of these 5 a hemicolectomy was also performed. The curves recorded were analyzed qualitatively and compared with curves from healthy intact control persons. In 9 patients distinct activity was recorded between 20 min and 3 1/2 hr after the operation and in 3 patients between 3 1/2 and 5 1/2 hr postoperatively. No difference was found between cholecystectomized and gastrectomized patients. In the 1 patient who had undergone duodenopancreatectomy, on the other hand, activity was delayed until 16 1/2 hr postoperatively. The initial contraction waves were predominantly of type I, and only in a few cases were type III waves seen. The propulsive motility was studied by following the point of maximal signal strength. Only 1-4 1/2 hr after cholecystectomies and gastric resections this point lay above the symphysis pubis or at the right or left iliac fossa, indicating that the propulsive intestinal motility of the small intestine was not notably reduced postoperatively. Only after extensive operations was a considerable decrease in this motility observed.

5872 LATERAL T-TUBE DUODENOSTOMY. DUODENAL STUMP MANAGEMENT AND MANOMETRICS. *(E.)* Dardik, I.; Dardik, H.; Shumofsky, E.; Gliedman, M. L. (Albert Einstein Coll. Med., New York, N.Y.). *Arch. Surg.* 107(1):89-90, 1973.

5873 INTESTINAL OBSTRUCTION IN THE NEWBORN. *(E.)* Shaw, A. (Univ. Virginia Med. Ctr., Charlottesville). *Paediatrician* 1(2):88-103, 1972/73.

5874 MECHANICAL SMALL BOWEL OBSTRUCTION. *(E.)* Levin, B. (Michael Reese Hosp. and Med. Ctr., Chicago, Ill.). *Semin. Roentgenol.* 8(3):281-297, 1973.

5875 RETROPERITONEAL AND TRANSMESOSIGMOID HERNIATION OF THE ILEUM. REPORT OF A CASE. *(E.)* Steele, Jr., G.; Sawyer, R. B.; Sawyer, K. C. (Univ. Colorado Sch. Med., Denver). *Rocky Mt. Med. J.* 70(6):30-32, 1973.

5876 CONGENITAL CAUSES OF DUODENAL OBSTRUCTION. *(E.)* Wilkinson, A. W. (Inst. Child Health, Univ. London, England). *J. R. Coll Surg. Edinb.* 18(4):197-208, 1973.

5877 INTRAMURAL HEMATOMA OF THE DUODENUM IN CHILDREN. REVIEW OF LITERATURE AND REPORT OF TWO CASES. *(E.)* Andersson, A.; Bergdahl, L. (Dept. Surg., Univ. Umea, Sweden). *Am. Surg.* 39(7):402-405, 1973.

5878 GASTROINTESTINAL NEUROPATHY IN FAMILIAL AMYLOIDOSIS. REPORT OF A CASE WITH SEVERE DIARRHEA WITHOUT STEATORRHEA OR MALABSORPTION. *(E.)* Carrizosa, J.; Lin, K. Y.; Myerson, R. M. (VA Hosp., Philadelphia, Pa.). *Am. J. Gastroenterol.* 39(6):541-546, 1973.

5879 ELECTROGASTROENTEROGRAPHY IN INFANTS. PRINCIPLE AND RESULTS IN INFANTS WITH NO DIGESTIVE DISORDERS. *(Fr.)* Thillier, J. L.; Combe, P. (Bretonneau Univ. Hosp. Ctr., Tours, France). *Pediatrie* 27(5):469-482, 1972.

5880 TREATMENT OF SEVERE FISTULAS OF THE SMALL INTESTINE. *(Fr.)* Maillet, P.; Cuche, J.; Micol, P.; Coffy, N. (no affil.). *J. Chir. (Paris)* 104(5):387-394, 1972.

5881 THE PATTERN OF INTRINSIC DUODENAL OBSTRUCTIONS. *(E.)* Reid, I. S. (Roy. Alexandra Children's Hosp., Camperdown, Australia). *Aust. N.Z. J. Surg.* 42(4):349-352, 1973.

5882 CONGENITAL SHORT BOWEL. *(E.)* Kern, I. B.; Harris, M. J. (Prince of Wales Hosp., Randwick, Australia). *Aust. N.Z. J. Surg.* 42(3): 283-285, 1973.

5883 PERFORATION OF THE SMALL INTESTINE SECONDARY TO LAPAROSCOPIC TUBAL CAUTERIZATION. *(E.)* Saltzstein, E. C.; Schwartz, S. F.; Levinson, C. J. (Mt. Sinai Med. Ctr., Milwaukee, Wis.). *Ann. Surg.* 178(1):34-36, 1973.

5884 LEIOMYOMA OF MECKEL'S DIVERTICULUM - PREOPERATIVE RADIOLOGIC DEMONSTRATION. CASE REPORT. *(E.)* Tabry, I. F.; Nassar, V. H.; Balikian, J. P. (Amer. Univ. Med. Ctr., Beirut, Lebanon). *Ann. Surg.* 178(1):31-33, 1973.

5885 CONGENITAL SHORT INTESTINE. A CASE REPORT AND REVIEW OF THE LITERATURE. *(E.)* Yutani, C.; Sakurai, M.; Miyaji, T.; Okuno, M. (Osaka Univ. Med. Sch., Japan). *Arch. Pathol.* 96(2):81-82, 1973.

5886 RARE CAUSES OF INTESTINAL OBSTRUCTION. (1). RETROGRADE JEJUNOGASTRIC INTUSSUSCEPTION. *(E.)* Newell, J. P.; Macintyre, I. M. C. (Victoria Hosp., Kirkcaldy, Scotland). *J. R. Coll. Surg. Edinb.* 18(4):231-233, 1973.

5887 INTRAOPERATIVE DECOMPRESSION OF THE OBSTRUCTED SMALL BOWEL. *(E.)* Wickstrom, P.; Haglin, J. J.; Hitchcock, C. R. (Minneapolis Med. Res. Fdn., Minn.). *Surgery* 73(2):212-219, 1973.

See also, 5772, 5780, 5791, 5848, 5896, 5924, 5928,
5938, 5959, 6066, 6123.

SMALL INTESTINE

Malabsorption

5888 ROLE OF BILE IN THE GENESIS OF MALABSORPTION IN PATIENTS WITH CHRONIC LIVER DISEASE. *(Sp.)* Solis Herruzo, J. A. (Fac. Med., Complutense Univ., Madrid, Spain). *Rev. Clin. Esp.* 125(4):301-312, 1972.

Liver biopsies were examined and lipids and bile acids determined on gallbladder bile from 6 normal subjects and 24 patients with liver disease. Patients were diagnosed as having chronic hepatitis (2), postnecrotic cirrhosis (5), chronic hepatitis developing into cirrhosis (3), cholelithiasis (5), septal cirrhosis (6), Dubin-Johnson syndrome (1), alcoholic hepatitis (1), and hepatic necrosis (1). Total bile acids were decreased in bile from patients with acute and chronic hepatitis, septal cirrhosis, and particularly postnecrotic cirrhosis. In general, the largest decreases occurred in glycocholic, glycohenodeoxycholic, glycodeoxycholic, and dihydroxycholic acids. No correlation was found between the extent of necrosis or cholestasis and the bile acid decrease but, with some exceptions, some correlations appear to exist between the severity of liver disease, inflammation, and destruction of lobular structure and the bile acid decrease in bile. Chemical characteristics incompatible with micelle formation were found in 3 of 6 patients with chronic hepatitis, 2 of 6 patients with septal cirrhosis, and 5 of 5 patients with postnecrotic cirrhosis.

5889 TREHALASE DEFICIENCY IN A FAMILY. *(E.)* Madzarovova-Nohejlova, J. (Fac. Med., Charles Univ., Plzen, Czechoslovakia). *Gastroenterology* 65(1):130-133, 1973.

A 24-yr-old white man was hospitalized with vomiting and diarrhea as a result of the ingestion of mushrooms (*Psalliota arvensis* and *Boletus edulis*). He became asymptomatic within 24 hr. The patient's father, uncle, and 2 cousins also had histories of mushroom intolerance. Small bowel biopsy, histological examination, and intestinal disaccharidases assay of the small bowel specimen, trehalase, and glucose tolerance tests were performed on the patient, his parents, brother, and 2 sisters. Complete absence of trehalase activity and trehalose intolerance were found in the patient and his father. This suggests a familial, perhaps genetic, nature of trehalase deficiency. An autosomal type of heredity is suggested.

5890 FAMILIAL GLUCOSE-GALACTOSE MALABSORPTION: REMISSION OF GLUCOSE INTOLERANCE.

(E.) Elsas, II., L. J.; Lambe, Jr., D. W. (Emory Univ. Sch. Med., Atlanta, Ga.). *J. Pediatr.* 83(2):226-232, 1973.

A homozygous affected child with familial glucose-galactose malabsorption had symptomatic remission from glucose-induced diarrhea. At 3 days of age she had presented with refractory diarrhea which remitted only on a diet free of glucose and galactose. During oral glucose tolerance tests conducted at 3 yr of age, she had glucorrhea, decreased intestinal transit time, and no increase in blood sugar values. Normal intestinal transit time with low but discernible rises in blood glucose were present following identical glucose loads at the age of 5 yr. The utilization of glucose and galactose by cultured skin fibroblasts and isolated peripheral erythrocytes was normal. However, *in vitro* sodium-dependent active transport of d-glucose by jejunal mucosa remained absent. No accumulation of glucose by a sucrase-dependent, sodium-independent jejunal transport system was present in the proband or in normal control subjects. Jejunal biopsy material was histologically normal. Anaerobic and aerobic cultures of jejunal succus entericus were comparable to those in controls. These data substantiate suggestions that clinical remission occurs with increased age in severe glucose-galactose malabsorption even though the jejunal mucosa remains unable to accumulate glucose by the active, sodium-dependent transport system.

5891 THE GASTROINTESTINAL ABSORPTION OF DIGOXIN IN SEVEN PATIENTS WITH GASTRIC OR SMALL INTESTINAL RECONSTRUCTIONS.

(E.) Beermann, B.; Hellstrom, K.; Rosen, A. (Dept. Med. Serafimerlasarettet, Stockholm, Sweden). *Acta Med. Scand.* 193(4):293-297, 1973.

Digoxin-12α-^{3}H and polyethylene glycol, unabsorbable marker, were given p.o. to 5 patients with partial gastrectomy, 1 patient with vagotomy and plastic reconstruction of the pylorus, and 1 with jejunocolostomy. A slight to moderate steatorrhoea was found in 4 of the patients with partial gastrectomy and in the 1 patient with jejunocolostomy. The ratio between the radioactivity/mg polyethylene glycol in intestinal aspirates and that of the test solution demonstrated that about 55% of the label was absorbed in the upper gastrointestinal tract of partial gastrectomy patients. This value and those recorded for blood levels and cumulative excretion of radioactivity in the urine were within the limits previously encountered in healthy control subjects. Although not indicated by the blood levels of label, the absorption of radioactivity appeared to be slightly impaired in 2 patients, the 1 with jejunocolostomy and the 1 with vagotomy and plastic reconstruction of the pylorus.

5892 BLOOD IN THE LYMPH (HEMOCHYLIA) AND INTESTINAL LYMPHANGIECTASIA ASSOCIATED WITH LUTEMBACHER'S SYNDROME.

(E.) Stalder, H.; Joliat, G. (Cantonal Hosp., La Chaux-de-Fonds, Switzerland). *Am. J. Med.* 55(1):99-104, 1973.

A 31-yr-old man presented with Lutembacher's syndrome (atrial septal defect and mitral stenosis) and protein-losing enteropathy. The protein-losing enteropathy was diagnosed by abnormal excretion of polyvinyl pyrrolidone in the stool, hypoproteinemia, and decreased half-life of radioactive albumin. Reversal of the protein-losing enteropathy 7 months after cardiac surgery suggested that the lymphangiectasis was secondary to the cardiac disorder, but it seems likely that the intestinal lymphangiectasia was not corrected. Spontaneous rupture of a congenital aneurysm of the splenic artery created a splenoportal arteriovenous fistula, causing a massive sequestration of blood into a grossly dilated, low-pressure abdominal lymphatic system; this facilitated development of massive hemochylia which resulted in hypovolemic shock and death.

5893 ILEAL BYPASS IN THE TREATMENT OF HYPERLIPOPROTEINAEMIA.

(E.) Thompson, G. R.; Gotto, Jr., A. M. (Baylor Coll. Med., Houston, Tex.). *Lancet* (7819):35-36, 1973.

The use of ileal bypass in types III and IV hyperlipoproteinemia is questioned since many of these patients respond to effective dietary and drug regimens. For similar reasons, patients with the non-familial variety of the type II disorder are not suggested as candidates for ileal bypass. In familial type II hyperlipoproteinemia it seems clear that the relatively rare but lethal homozygous form of this disorder is as resistant to ileal bypass as it is to all other treatment. However, patients with the heterozygous type II disorder vary considerably in their response to hypocholesterolemic agents. Many type II patients respond to cholestyramine, nicotinic acid, neomycin, or D-thyroxine. Although ileal bypass is undoubtedly an effective way of lowering the serum cholesterol in hyperlipoproteinemic patients, diet in conjunction with cholestyramine is also effective. It is suggested that the choice depends on factors such as cost, tolerance of medication, surgical risks, and the

ersonal desires of the patient. It is stressed that
prophylactic ileal bypass operation may not be the
ethod of choice for controlling hyperlipoproteinemia
growing children or in other individuals with the
ype II disorder. It is suggested that the operation
e limited to young adult patients with severe
eterozygous type II hyperlipoproteinemia which has
roven refractory to drugs or to patients unable to
olerate an effective drug regimen.

394 THE EFFECT OF COELIAC DISEASE UPON BILE SALTS. *(E.)* Low-Beer, T. S.; Heaton,
. W.; Pomare, E. W.; Read, A. E. (Bristol Roy.
nfirm., England). *Gut* 14(3):204-208, 1973.

e size and composition of the bile salt pool has
een measured in 14 patients with untreated celiac
isease and in 17 control subjects. The total bile
lt pool was markedly increased in celiac patients,
e average being 9.2 g compared with 3.1 g in controls.
e average taurocholate pool was 1114 mg in celiac
tients, 3 times the average for controls. Tauro-
olate synthesis was normal, consistent with its
larged pool and prolonged half-life. Half-life
d pool size were significantly correlated. The
mposition of the bile salt pool was virtually
entical in the two groups. It is suggested that
the enterohepatic circulation is slowed by gall-
adder inertia, bile salts are less effectively
d back to the liver and consequently hepatic mon-
oring of pool size is diminished.

395 SIMULTANEOUS MEASUREMENT OF FREE AND INTRINSIC FACTOR (IF) BOUND VITAMIN B_{12}
$_{12}$) ABSORPTION: ABSOLUTE QUANTITATION WITH INCOM-
ETE STOOL COLLECTION AND RAPID RELATIVE MEASURE-
NT USING PLASMA B_{12} (IF): B_{12} ABSORPTION RATIO.
.) Fish, M. B.; Pollycove, M.; Wallerstein, R. O.;
eng, K. K. S.; Tono, M. (Univ. California Sch.
d., San Francisco). *J. Nucl. Med.* 14(8):568-
5, 1973.

5896 THE PATHOPHYSIOLOGICAL CONSEQUENCES OF THE REVERSAL OF AN INTESTINAL LOOP. *(Fr.)* Grenier, J. F.; Jaeck, D.; Sava, G.; Dauchel, J.; Eloy, M. R. (Civ. Hosp., Strasbourg, France). *Acta Gastroenterol. Belg.* 36:92-104, 1973.

5897 HEREDITARY ALTERATIONS OF FRUCTOSE METABOLIZING ENZYMES. *(E.)* Schapira, F.; Nordmann, Y.; Gregori, C. (Inst. Molec. Pathol., Paris, France). *Acta Med. Scand. (Suppl.)* 542: 77-83, 1972.

5898 HEREDITARY FRUCTOSE INTOLERANCE. *(E.)* Perheentupa, J.; Raivio, K. O.; Nikkila, E. A. (Children's Hosp., Univ. Helsinki, Finland). *Acta Med. Scand. (Suppl.)* 542:65-75, 1972.

5899 SUPERIOR MESENTERIC ARTERY EMBOLECTOMY. SHORT BOWEL SYNDROME TREATED BY REVERSAL OF INTESTINE. *(E.)* Man, B.; Kraus, L.; Czerniak, P. (Meir Hosp. Kfar Sava, Israel). *Vasc. Surg.* 7(3):176-180, 1973.

5900 ENVIRONMENTAL CORRELATES OF SEVERE CLINICAL MALNUTRITION AND LANGUAGE DEVELOPMENT IN SURVIVORS OF KWASHIORKOR OR MARASMUS. *(E.)* Cravioto, J.; DeLicardie, E. (Hosp. Infantil de la IMAN, Mexico City). *Bol. Of. Sanit. Panam.* 7(2):50-70, 1973.

See also, 5749, 5784, 5944.

LARGE INTESTINE

01 ARTERIOGRAPHIC DIAGNOSIS AND MANAGEMENT OF SUSPECTED COLONIC DIVERTICULAR HERMORRHAGE.
.) Eisenberg, H.; Lauffer, I.; Skillman, J. J.
arvard Med. Sch., Boston, Mass.). *Gastroenterology*
(6):1091-1100, 1973.

elective arteriography was performed in 12 patients
th rectal hemorrhage who were suspected of having
verticulosis as the cause of bleeding. The
teriogram was negative in 4 patients and these 4 have had no recurrence of hemorrhage. In 4 patients, the hemorrhage was due to a lesion other than diverticulosis: malignant lymphoma, intestinal ischemia, cecal ulcer, and arteriovenous malformation of the small bowel. Bleeding from diverticular disease of the colon occurred in 4 patients, including 3 with diverticulosis and 1 with diverticulitis. Of these patients, 3 were treated with intraarterial infusion of vasopressin (0.2-0.3 U/ml/min infused for 4-12 hr). In each case

bleeding stopped for at least 24 hr resulting in significant improvement in the preoperative condition of these patients. Selective arteriography in patients in whom hemorrhage is thought to be due to colonic diverticular disease is indicated to exclude other causes of rectal hemorrhage, accurately localize the site of the bleeding diverticulum, allow a trial of nonoperative control of hemorrhage by infusion of vasopressin or other vasoconstrictor agents, and allow more specific and limited colonic resection when bleeding is uncontrolled or recurrent.

5902 LYMPHOCYTE TRANSFORMATION IN LARGE BOWEL CANCER. *(E.)* Lauder, I.; Bone, G. (Dept. Pathol. Univ. Newcastle Upon Tyne, England). *Br. J. Cancer* 27(5):409-413, 1973.

Lymphocyte transformation in 21 patients (aged 39-81 yr) with adenocarcinoma of the colon and rectum was measured by uptake of [^{14}C] thymidine. A whole blood microculture technique was used to determine dose response curves in patients and healthy controls. Whole blood (10 ml) was obtained by venepuncture and placed in a tube with 400 U of preservative free heparin. Blood was added to medium 199 containing penicillin, streptomycin, and neomycin supplemented with 20% pooled human AB serum to give a final concentration of 2 x 10^5 lymphocytes/5 ml volume. To 5 ml aliquots, 0.1-3000 μg phytohemagglutinin were added in 0.1 ml volumes, followed by 0.15 μCi [^{14}C] thymidine. The pattern of lymphocyte transformation was similar in patient and control tests up to the 10 μg dose level of phytohemagglutinin. The curve for cancer patients flattened off beyond the 40 μg point to reach a peak of 2373 counts/min at 100 μg, whereas in normal controls the uptake of thymidine at 100 μg was 6192 counts/min with a peak of 7674 counts/min occurring at 1000 μg. Thus, there is a statistically highly significant depression in lymphocyte transformation in this group of cancer patients, and this depressed response may well be due to an intrinsic cellular defect.

5903 RETRORECTAL CYSTS OF DEVELOPMENTAL ORIGIN. *(E.)* Campbell, W. L.; Wolff, M. (Columbia-Presbyterian Med. Ctr., New York, N.Y.). *Am. J. Roentgenol. Radium Ther. Nucl. Med.* 117(2):307-313, 1973.

Developmental retrorectal cysts were noted in 4 patients including 3 females aged 20-30 yr. In 1 case, difficulty did not occur until a rectal tumor was discovered during delivery of the third child. A cystic mass was removed 2 yr later and the pathologic diagnosis was postanal gut cyst, inflamed. In the 2nd case, a right perirectal abscess developed after her first delivery. After 4 yr a cystic fluid-filled retrorectal mass was excised and the pathologic diagnosis was duplication of the rectum. The 3rd case developed an abscess near the tip of the coccyx. Perirectal cysts were excised after 5 yr; 2 months later an inflamed retrorectal cyst was excised. A cyst of the posterior wall of the rectum below the tip of the coccyx was excised 1 yr later. Pathological diagnosis was a cyst of congenital origin lined by stratified squamous epithelium. Hemorrhoidectomy was performed on the 4th patient, a 61 yr old male. After 7 yr a retrorectal cyst with its sinus tract was excised. The pathologic diagnosis was a cyst lined by stratified squamous epithelium with inflammatory changes. Barium enema may reveal smooth mass effects on the posterior rectal wall anterior to the coccyx and lower sacrum. Sinograms may detect infected cysts which develop fistulous tracts to the rectum and the skin between the anus and coccyx. Roentgenograms may aid in differentiating developmental cysts from other mass lesions of the retrorectal space.

5904 RADIATION-INDUCED CARCINOMA OF THE TRANSVERSE COLON: REPORT OF A CASE. *(E.)* Cunningham, M. P.; Wilhoite, R. (St. Francis Hosp., Evanston, Ill.). *Dis. Colon. Rectum* 16(2):145-148, 1973.

5905 RESULTS OF SURGICAL THERAPY OF RECTAL PROLAPSE. *(Rus.)* Gel'fenbein, L. S.; Uskov, A. G. (no affil.). *Vestn. Khir.* (5):45-48, 1972.

5906 ADENOMATOUS POLYP WITH SUBMUCOSAL CYSTS. *(E.)* Fechner, R. E. (Baylor Coll. Med., Houston, Tex.). *Am. J. Clin. Pathol.* 59:498-502, 1973.

5907 MALIGNANT GIANT-CELL TUMOUR OF THE COLON. *(E.)* Eshun-Wilson, K. (Odense Univ. Hosp., Denmark). *Acta Pathol. Microbiol. Scand. [A]* 81(2):137-144, 1973.

5908 THE SPECIFICITY OF THE CHROMOSOMAL ABNORMALITIES IN HUMAN COLONIC POLYPS. A CYTOGENETIC STUDY OF MULTIPLE POLYPS IN A CASE OF GARDNER'S SYNDROME. *(E.)* Mark, J.; Mitelman, F.; Dencker, H.; Norryd, C.; Tranberg, K.-G. (Huddinge Hosp., Lund, Sweden). *Acta Pathol. Microbiol. Scand. [A]* 81(1):85-90, 1973.

5909 IRRITABLE COLON: IRRELEVANT FINDING OR IMPORTANT DIAGNOSIS? *(Ger.)* Swart, B.; Vielhauer, E. (Lukas Hosp., Neuss, Germany). *Radiologe* 12(6):179-184, 1972.

5910 GANGRENE AND PERFORATION OF THE APPENDIX ASSOCIATED WITH SHIGELLOSIS AND SALMONELLOSIS. *(Cz.)* Jiran, B. (OUNZ, Kolin, Czechoslovakia). *Rozhl. Chir.* 51(7):427-430, 1972.

5911 BLOOD BORNE METASTASIS IN CARCINOMA OF THE LARGE INTESTINE. *(E.)* Nahra, K. S. (no affil.). *J. Med. Liban.* 25(6):447-452, 1972.

5912 NEW METHODS FOR DIAGNOSING AND TREATING PARAPROCTITIS. *(Rus.)* Zaremba, A. A. (Riga Munic. Clin. Hosp. Emergency Treatment, USSR). *Eksp. Khir. Anesteziol.* 17(3):32-35, 1972.

5913 COLONIC RETENTION SYNDROME (MEGACOLON) ASSOCIATED WITH IMMATURITY OF INTESTINAL PLEXUS. *(E.)* Emery, J. L. (Children's Hosp., Sheffield, England). *Proc. R. Soc. Med.* 66(3): 222-223, 1973.

5914 A CRITICAL LOOK AT THE SOAVE PROCEDURE FOR HIRSCHSPRUNG'S DISEASE. *(E.)* Deodhar, M.; Sieber, W. K.; Kiesewetter, W. B. (Univ. Pittsburgh Sch. Med., Pa.). *J. Pediatr. Surg.* 8(2): 249-254, 1973.

5915 ACUTE APPENDICITIS IN THE FIRST TWO YEARS OF LIFE. *(E.)* Grosfeld, J. L.; Weinberger, M.; Clatworthy, Jr., H. W. (Ohio State Univ. Coll. Med., Columbus). *J. Pediatr. Surg.* 8(2):285-293, 1973.

5916 CARCINOID TUMORS OF THE APPENDIX. REPORT OF THIRTY-FIVE CASES. *(E.)* Ponka, J. L. (Henry Ford Hosp., Detroit, Mich.). *Am. J. Surg.* 126(1):77-83, 1973.

5917 SUBCUTANEOUS EMPHYSEMA OF GASTROINTESTINAL ORIGIN: REPORT OF FOUR CASES. *(E.)* Dharia, K. M.; Shah, I. C. (Brooklyn-Cumberland Med. Ctr., N.Y.). *Dis. Colon Rectum* 16(4):319-324, 1973.

5918 DUPLICATION OF THE RECTUM: REPORT OF A CASE. *(E.)* Ruiz Moreno, F.; Ruiz Healy, F. (no affil.). *Dis. Colon Rectum* 16(4):315-318, 1973.

5919 SUPPURATIVE PYLEPHLEBITIS AND LIVER ABSCESS COMPLICATING COLONIC DIVERTICULITIS: REPORT OF TWO CASES AND REVIEW OF LITERATURE. *(E.)* Lin, C. S. (City Hosp. Ctr., Elmhurst, N.Y.). *Mt. Sinai J. Med. N.Y.* 40(1):48-55, 1973.

5920 ABSCESS OF THE ABDOMINAL WALL AS THE PRESENTING SIGN IN CARCINOMA OF THE COLON. *(E.)* White, A. F.; Haskin, B. J.; Jenkins, C. K.; Pfister, R. C. (Harvard Med. Sch., Boston, Mass.). *Cancer* 32(1):142-146, 1973.

5921 APPENDICITIS AND THE ABDOMINAL ROENTGENOGRAM IN CHILDREN. *(E.)* Hatten, L. E.; Miller, R. C.; Hester, Jr., C. L.; Moynihan, P. C. (Univ. Mississippi Med. Ctr., Jackson). *South. Med. J.* 66(7):803-806, 1973.

5922 AN UNUSUAL CASE OF LARGE BOWEL OBSTRUCTION. *(E.)* Louw, J. X.; (Ashburton Hosp., Australia). *N.Z. Med. J.* 76(483):107-108, 1972.

5923 DIAGNOSTIC AND THERAPEUTIC COLOSCOPY: A NEW APPROACH TO MANAGEMENT OF COLON POLYPS. *(E.)* Hogan, W. J.; Geenen, J. E.; De Cosse, J. J. (Med. Coll. Wisconsin, Milwaukee). *Wis. Med. J.* 72(3):101-102, 1973.

5924 ROENTGENOGRAPHIC MANIFESTATIONS OF IMMATURITY OF THE INTESTINAL NEURAL PLEXUS IN PREMATURE INFANTS. *(E.)* Vanhoutte, J. J.; Katzman, D. (Univ. Colorado Med. Ctr., Denver). *Radiology* 106(2):363-367, 1973.

5925 CONCERNING THE DIAGNOSIS IN CANCER OF THE COLON AND RECTUM. *(Rus.)* Judin, I. J.; Nurov, A. V. (USSR Acad. Med. Sci., Moscow). *Vopr. Onkol.* 18(10):75-79, 1972.

5926 HEMORRHAGE FROM CECAL ULCERS OF CYTOMEGALOVIRUS INFECTION: REPORT OF A CASE. *(E.)* Wolfe, B. M.; Cherry, J. D. (Saint Louis Univ. Sch. Med., Mo.). *Ann. Surg.* 177(4): 490-494, 1973.

5927 GIANT SOLITARY DIVERTICULUM OF THE TRANSVERSE COLON WITH DIVERTICULOSIS. *(E.)* Sagar, S. (Derby City Hosp., England). *Br. J. Clin. Pract.* 27(4):145-146, 1973.

5928 SEGMENTAL TUBERCULOSIS OF THE COLON WITH ENTERO-COLIC FISTULA. *(E.)* Patel, M. P.; De, I. (Coventry Group Hosp., England). *Br. J. Radiol.* 45(530):150-152, 1972.

5929 THE ROLE OF SUTURES IN RECURRENCE OF CARCINOMA AT THE SITE OF INTESTINAL ANASTOMOSIS. *(E.)* Douglass, H. O.; Leveen, H. H. (Downstate Med. Ctr., State Univ. New York, Brooklyn). *Exp. Med. Surg.* 29(1-2):89-95, 1973.

See also, 5764, 5770, 5775, 5787, 5793, 5798, 5866, 5870, 5873, 5878, 5937, 5939, 6093, 6112, 6117, 6119, 6128.

LARGE INTESTINE

Ulcerative Colitis

5930 THE METABOLISM OF SALICYAZOSULPHAPYRIDINE IN ULCERATIVE COLITIS. II. THE RELATIONSHIP BETWEEN METABOLITES AND THE PROGRESS OF THE DISEASE STUDIED IN OUTPATIENTS. *(E.)* Das, K. M.; Eastwood, M. A.; McManus, J. P. A.; Sircus, W. (Western Gen. Hosp., Edinburgh, Scotland). *Gut* 14(8):637-741, 1973.

Serum concentrations of salicylazosulfapyridine, sulfapyridine, and 5-aminosalicylic acid were measured in 64 outpatients with ulcerative colitis. About 90% of the patients in remission had serum total sulfapyridine concentrations above 20 μg/ml. However, 7 patients had active disease despite a serum total sulfapyridine concentration > 20 μg/ml. The salicylazosulfapyridine and the individual sulfapyridine metabolites did not show any correlation with the disease state. The most effective dose of salicylazosulfapyridine was 3 g/day for slow acetylators, 2 g/day may be adequate. Plain and enteric-coated tablets produced similar concentrations at equivalent dosage. Side effects due to salicylazosulfapyridine were frequent in patients who had a total sulfapyridine concentration > 50 μg/ml of serum. Side effects included blue discoloration of serum and mucosa (4 patients), transient reticulocytosis (3), and haemolysis (1). Of these 8 patients, 4 were taking 4 g or more and 2 were taking 3 g of salicylazosulfapyridine/day.

5931 VIRAL INVESTIGATIONS IN ULCERATIVE COLITIS AND REGIONAL ENTERITIS. *(E.)* Farmer, G. W.; Vincent, M. M.; Fuccillo, D. A.; Horta-Barbosa, L.; Ritman, S.; Sever, J. L.; Gitnick, G. L. (Sch. Med., Univ. California, Los Angeles). *Gastroenterology* 65(1):8-18, 1973.

Sera from 57 patients with ulcerative colitis, 15 patients with regional enteritis, and 65 age-, race-, and sex-matched control subjects, were tested for the presence of antibodies to viral antigens. A higher frequency of cytomegalovirus antibody and higher cytomegalovirus titers were found in patients. The presence or absence of a history of prior blood transfusions or steroid treatment did not affect the distribution of cytomegalovirus antibody among the groups studied. Tissue specimens from ulcerative colitis patients, regional enteritis patients, and control subjects were grown in tissue culture. Of 6 ulcerative colitis patients and 1 of 4 regional enteritis patients had cytomegalovirus present in tissue culture as determined by cytopathic effect, indirect fluorescent antibody tests, and electron microscopy. Furthermore, cell pack preparations from these infected cell lines reacted specifically with cytomegalovirus antibody in complement fixation. Tissue culture from 1 patient underwent spontaneous malignant transformation. Cytomegalovirus may actively replicate in the bowel wall of patients with inflammatory bowel disease. Evidence of cytomegalovirus infections is common among ulcerative colitis patients, whereas chronically ill regional enteritis patients develop antibody as frequently as do control subjects. These results suggest that tissue culture techniques may be valuable in investigating the role of viruses in inflammatory bowel diseases. Although no evidence exists that cytomegalovirus takes part in the pathogenesis of ulcerative colitis or regional enteritis, it is suggested that cytomegalovirus may be involved in causing, exacerbating, or prolonging exacerbations of these 2 diseases or may contribute to their neoplastic potential.

5932 A DISCORDANT OCCURRENCE OF ULCERATIVE COLITIS IN IDENTICAL TWINS. *(E.)* Qazi, Q. H.; Piken, E.; Fierst, S. (Downstate Med. Ctr., State Univ. New York, Brooklyn). *Gastroenterology* 65(1): 134-136, 1973.

Active chronic ulcerative colitis was diagnosed in a 61-yr-old female monozygotic twin of Ashkenazi Jewish descent, who had suffered recurrent bouts of bloody and mucous diarrhea for 11 yr. Polypectomy was performed and histological examination revealed granulation tissue indicative of a pseudopolyp. One month later ulcerative colitis was reconfirmed and medical management with corticosteroids, corticotropin, and salicylazo-sulfapyridine commenced. After 5 months a rectovaginal fistula developed followed 1 month later by perianal fistula and anal ulcer. A total proctocolectomy and ileostomy were performed. There is no history of gastrointestinal disease or ankylosing spondylitis in any member of the family, including the other twin. The other twin has remained healthy for 12 yr since the appearance of the disease in her sister. The normal twin has no symptoms related to liver or joints and thus, this condition had not expressed itself in any manner. In contrast to other studies, these twins are discordant for ulcerative colitis. This discordance in a set of monozygotic twins strengthens the hypothesis that ulcerative colitis is not inherited as a single dominant or recessive gene with full penetrance.

5933 DECREASED TRANSMURAL POTENTIAL DIFFERENCE ACROSS THE HUMAN RECTUM IN ULCERATIVE COLITIS. *(E.)* Rask-Madsen, J.; Dalmark, M. (Glostrup Hosp., Denmark). *Scand. J. Gastroenterol.* 31(3): 321-326, 1973.

At routine sigmoidoscopy, during perfusion of the rectum or after perfusion of the entire colon for 3-6 hrs, the electrical potential difference across the rectal wall was measured in 53 healthy subjects and in 31 patients (aged 20-64 yr) with ulcerative colitis. The results obtained in healthy subjects demonstrated that application of the exploring salt bridge directly on the mucosa and the reference electrode i.v. caused less interindividual variations than previously assumed. The transmural potential difference was reduced in all patients and approached zero in severe attacks, while the polarity of the luminal surface never reversed. The significance of abnormal electrical characteristics in colonic inflammatory disease is difficult to interpret. However, a reliable and sensitive method of potential difference measurement may have some diagnostic potential.

5934 LYMPHOCYTE RESPONSES TO NONSPECIFIC MITOGENS IN INFLAMMATORY BOWEL DISEASE. *(E.)* Asquith, P.; Kraft, S. C.; Rothberg, R. M. (Dept. Med.,
niv. Chicago, Ill.). *Gastroenterology* 65(1):1-7,
973.

To assess cell-mediated immunity, circulating lympho-
cytes from 27 patients with inflammatory bowel disease,
and 24 healthy control subjects were cultured in the
resence of multiple doses of phytohemagglutinin,
oncanavalin A, and pokeweed mitogen. Of the 27 pa-
ients, 13 (aged 16-63 yr) had Crohn's disease (7
ith ileocolitis, 3 with regional enteritis, and 3
ith evidence of recurrent disease after bowel resec-
ion and ileotransverse colostomy). The remaining 14
atients (aged 16-71 yr) had ulcerative colitis (8
ith involvement of the entire colon, 5 with only
eft-sided disease, and 1 with ulcerative proctitis).
here was considerable variation in the results with
arked overlap among the 3 groups of subjects, and
uch variability existed as to the optimal dose of a
itogen needed to elicit a maximal response in a
iven subject. Several of the patients with either
ype of inflammatory bowel disease had poor lympho-
yte responses, but no significant differences were
emonstrated among the 3 groups. There was a trend
owards poorer lymphocyte responsiveness in patients
ith Crohn's disease of moderate to severe clinical
ctivity. Since equally low values also were found
n healthy individuals, such isolated *in vitro* obser-
ations are in themselves inadequate bases upon which
o draw etiological or pathogenetic conclusions.

935 ON THE AETIOLOGY OF ULCERATIVE COLITIS. A VASCULAR HYPOTHESIS. *(E.)* Fairburn,
. A. (Middlesex Hosp. Med. Sch., London, England).
ancet (7805):697-699, 1973.

936 INTRAMURAL BARIUM (BARIUM GRANULOMA) OF COLON AND RECTUM. *(E.)* Carney, J. A.;
tephens, D. H. (Mayo Clin., Rochester, Minn.).
stroenterology 65(2):316-320, 1973.

37 LINITIS PLASTICA (SIGNET-RING CELL) CARCINOMA OF THE COLON IN ULCERATIVE COLITIS.
.) Corman, M. L.; Rosenoer, V. M.; Barr, R.
ahey Clin. Fdn., Boston, Mass.). *Lahey Clin.*
nd. Bull. 22(1):17-22, 1973.

38 ULCERATIVE COLITIS AND ULCERATIVE GASTRITIS. *(E.)* Manier, J. W.; Reyes,
N.; Olsen, T. G. (Marshfield Clin., Wis.).
. J. Gastroenterol. 58(5):502-507, 1972.

5939 ULCERATIVE COLITIS PROXIMAL TO CARCINOMA OF THE COLON. *(E.)* Campbell, J. B. (Children's Hosp., Denver, Col.). *Rocky Mt. Med. J.* 70(5):50-52, 1973.

5940 CEREBRAL VENOUS THROMBOSIS IN ULCERATIVE COLITIS. *(E.)* Borda, I. T.; Southern, R. F.; Brown, W. F. (St. Joseph's Hosp., London, Canada). *Gastroenterology* 64(1):116-119, 1973.

5941 OUTPATIENT THERAPY OF ULCERATIVE COLITIS. *(Ger.)* Reitzig, P.; Lisewski, G. (1st Med. Clin., Humboldt Univ., Berlin, Germany). *Dtsch. Gesundheitsw.* 27(36):1717-1719, 1972.

5942 IMMUNOLOGICAL STUDIES IN ULCERATIVE COLITIS. *(Ger.)* Gulke, L.; Kettner, W. (Regional Hosp., Cottbus, Germany). *Z. Gesamte Inn. Med.* 27(9):403-405, 1972.

5943 MORTALITY ASSOCIATED WITH ULCERATIVE COLITIS. *(E.)* Hughes, E. S. (Roy. Melbourne Hosp., Australia). *Med. J. Aust.* 2(18):1009-1010, 1972.

See also, 5767, 6114, 6118.

5944 TRYPSIN-LIKE NATURE OF THE PANCREATIC FACTOR THAT CORRECTS VITAMIN B_{12} MALABSORPTION ASSOCIATED WITH PANCREATIC DYSFUNCTION. *(E.)* Toskes, P. P.; Deren, J. J.; Conrad, M. E. (Walter Reed Army Inst. Res., Washington, D.C.). *J. Clin. Invest.* 52(7):1660-1664, 1973.

Hog pancreas was subfractionated and assessed for its ability to correct vitamin B_{12} malabsorption in patients with pancreatic dysfunction and in rats with partial pancreatic extirpation. The constitutent obtained from the pancreas that increased vitamin B_{12} absorption in both humans and rats was soluble at 50,000 gravity, heat labile, acid stable, and approximately 20,000-25,000 in molecular weight. The active subfractions contained tryptic and chymotryptic but no amylase or lipase activity. Thrice-crystallized trypsin (10 mg) corrected the vitamin B_{12} malabsorption in 2 patients with pancreatic insufficiency and in rats with subtotal pancreatectomy. These data indicate that pancreatic proteolytic enzymes—in particular, trypsin--are necessary for optimal vitamin B_{12} absorption. It seems that neither gastric intrinsic factor nor the ileal receptor needs a pancreatic factor to be biologically active. Instead, the pancreactic factor may act in the lumen of the gastrointestinal tract to keep the gastric intrinsic factor-vitamin B_{12} complex in a readily absorbable form.

5945 CYSTIC FIBROSIS: TRADITIONAL AND RECENT CONCEPTS. *(E.)* Gibbs, G. E. (Univ. Nebraska Coll. Med., Omaha). *Paediatrician* 1(3): 133-145, 1972/73.

5946 POSSIBLE GENETIC LINKS BETWEEN CYSTIC FIBROSIS OF THE PANCREAS AND ASPIRIN SENSITIVE ASTHMA. *(E.)* Caplin, I.; Haynes, J. T. (no affil.). *Ann. Alergy* 31(7):320-327, 1973.

5947 BENIGN HEMANGIOENDOTHELIOMA OF THE HEAD OF THE PANCREAS TREATED BY PANCREATICODUODENECTOMY. *(E.)* Chappell, J. S. (no affil.). *J. Pediatr. Surg.* 8(3):431-432, 1973.

5948 THE LATE GASTROINTESTINAL MANIFESTATIONS OF CYSTIC FIBROSIS OF THE PANCREAS. *(E.)* Berk, R. N.; Lee, F. A. (Univ. California, Sch. Med., San Diego). *Radiology* 106(2):377-381, 1973.

5949 GASTROINTESTINAL BLEEDING CAUSED BY AN ABERRANT PANCREAS. *(Fr.)* Prandi, D.; Fekete, F.; Lortat-Jacob, J. L. (Beaujon Hosp., Clichy, France). *Med. Chir. Dig.* 1(1):33-35, 1972.

5950 PANCREATIC TRANSPLANTATION. *(E.)* Kapoor, B. M. L. (All India Inst. Med. Sci., New Dehli). *Q. J. Surg. Sci.* 8(3):119-122, 1972.

5951 ADENOCARCINOMA OF THE PANCREAS. A REVIEW OF 100 CASES. *(E.)* Grieve, D. C. (Western Gen. Hosp., Edinburgh, Scotland). *J. R. Coll. Surg. Edinb.* 18(4):221-226, 1973.

5952 ANNULAR PANCREAS IN AN ADULT. *(E.)* Mendelson, G.; Kotzmann, R. R.; McLellan, R. M.; Nayman, J. (Southern Mem. Hosp., Victoria, Australia). *Aust. N.Z. J. Surg.* 42(3):278-283, 1973.

5953 DIFFERENTIAL DIAGNOSIS OF PANCREATIC CALCIFICATION. *(E.)* Ring, E. J.; Eaton, Jr., S. B.; Ferrucci, Jr., J. T.; Short, W. F. (Harvard Med. Sch., Boston, Mass.). *Amer. J. Roentgenol. Radium Ther. Nucl. Med.* 177(2): 446-452, 1973.

5954 CLINICAL SEGMENTAL PANCREATIC TRANSPLANTATION WITH URETER-PANCREATIC DUCT ANASTOSIS FOR EXOCRINE DRAINAGE. *(E.)* Gliedman, M. L.; Gold, M.; Whittaker, J.; Rifkin, H.; Soberman, R.; Freed, S.; Tellis, V.; Veith, F. J. (Montefiore Hosp., Bronx, N.Y.). *Surgery* 74(2):171-180, 1973.

See also, 5785.

PANCREAS

Pancreatitis

5955 ANGIOGRAPHIC DIAGNOSIS OF INFLAMMATORY DISEASE OF THE PANCREAS. *(E.)* Tylen, U.; Arnesjo, B. (Univ. Hosp., Lund, Sweden). *Acta Radiol. (Diagn.)* 14(2):215-240, 1973.

Over a 10-yr period, 87 patients (64 males and 23 females) with pancreatitis were examined by angiography. These patients included 43 with chronic pancreatitis, 28 with acute pancreatitis, and 16 with relapsing pancreatitis. The most common finding in patients with chronic pancreatitis was increased tortuosity of the pancreatic arcades and intrapancreatic arteries (38

patients) followed by regular stenotic changes (36 pa-
tients), and changes in the splenic vein (23). Other
changes included arterial spasms (9), arterial aneu-
rysms (4 patients), and displacement because of an
abscess or pseudocyst (6) or retroperitoneal adhesions
(4). Vascularization of the pancreas was increased
in 18 patients and decreased in 15 patients. Although
vascular changes occurred with almost equal frequency
in patients with pancreatic calcification (17) and
those without, vascularization of the pancreas was
more often reduced with pancreatic calcification.
Vascular changes became more pronounced and stenotic
arterial changes extended to more arteries with in-
creasing duration of the pancreatitis. Of the 28 pa-
tients with acute pancreatitis, 18 had arterial steno-
sis, 22 had tortuosity of intrapancreatic arteries, 2
had arterial aneurysms, and 1 had arterial spasms.
The splenic vein was compressed in 10 and occluded in
patients. Arterial displacement was caused by a
pseudocyst or abscess in 8 of 9 patients. Vasculariza-
tion of the pancreas was increased in 8 and decreased
n 5 patients. Vascular changes associated with bi-
iary tract disease, which was regarded as a possible
ause of pancreatitis in 9 of these patients, differed
ittle from those in patients without biliary tract
isease. Of the 16 patients with relapsing pancrea-
itis, 10 had tortuosity of the pancreatic arteries,
0 had arterial stenosis, 7 had arterial spasm, 1 had
n aneurysm of the splenic artery, and 6 had involve-
ment of the splenic vein (compression in 3 and occlu-
ion in 3). Vascular displacement resulted from a
seudocyst or abscess in 3 patients. Vascularization
f the pancreas was increased in 5 and decreased in 6
atients. Vascular changes increased with the dura-
ion of the disease and particularly with the number
f attacks; the most marked increase was in venous
esions. However, the frequency of stenotic changes
n arteries surrounding the pancreas and of tortuosity
nd lumen irregularities in pancreatic arteries also
ncreased. Attempts to distinguish between a pseudo-
yst and an abscess by angiography alone were unsuc-
essful. When evaluating the angiographic findings
onsideration of the type and phase of pancreatic
isease is of the utmost importance.

956 TREATMENT OF PAIN IN CHRONIC PANCREATITIS BY IRRADIATION. *(E.)* Werner, G.; Wetter-
ors, J. (Dept. Surg., Karolinska Sjukhuset, Stock-
olm, Sweden). *Acta Radiol.* [*Ther.*] *(Stockh.)* 12(1):
-16, 1973.

oses of high-voltage irradiation were given to 9
atients (5 males and 4 females, aged 33-60 yr)
uffering from chronic pancreatitis. Biliary di-
ease was indicated in the histories of 2 patients;
eptic ulcer in 3, 1 of whom also had biliary di-
ease; and alcoholism in 4, 1 of whom also had peptic
lcer. In 2 patients 200 kilo/Volt radiation was
iven with a Thoreus filter, 4 received ^{60}Co kilo-
urie, and 3 received 6 milliVolt radiation from a
inear accelerator. A misdiagnosis of pancreatic
arcinoma caused 1 patient to receive 5000 rad as
site dose to the pancreas over 56 days. Other
atients received 1000-2050 rad over 15-33 days.
Recurrence of pain in 2 cases caused retreatment in each. In 6 patients complete relief of pain for a period of at least 2 yr was achieved. In 4 of 6 patients receiving 1500-2000 rad, the pancreatic enzyme determination after stimulation with secretin diminished to 1/3 to 1/2 that recorded before irradiation. Noted diabetes disappeared from the patient receiving 5000 rad. The endocrine pancreatic function was unaffected in the other 8. Although, 5 patients complained of exhaustion, for some months after treatment, only 1 serious side effect, gastritis, was noted, and it occurred in a patient with peptic ulcer history. It is, therefore, suggested that radiation therapy be further evaluated for use in cases of painful chronic pancreatitis. Alleviation of pain was greatest in those patients in whom the pancreatic exocrine function before treatment was low.

5957 POST-TRAUMATIC ACUTE HEMORRHAGIC PANCREATITIS: VALUE OF THE "COLON CUT-OFF" SIGN. *(E.)* Zanca, P.; Cody, T. J. (Univ. Texas Med. Sch., San Antonio). *Clin. Med.* 80(6):15-19, 1973.

5958 A COMPARATIVE STUDY OF EXOCRINE AND ENDOCRINE FUNCTIONS OF THE PANCREAS IN PATIENTS WITH CHRONIC PANCREATITIS. *(Fr.)* Descos, L.; Bizollon, C. A.; Faure, A.; Phelip, E.; Berger, G.; Vagne, M.; Lambert, R. (E. Herriot Hosp., Lyon, France). *Arch. Fr. Mal. App. Dig.* 62(2):113-123, 1973.

5959 PYLORO-DUODENAL STENOSIS FOLLOWING PANCREAS SURGERY IN CHRONIC PANCREATITIS. *(Fr.)* Sarles, J. C.; Guily, J. (Hotel Dieu, Marseille, France) *Arch. Fr. Mal. App. Dig.* 62(2):151-156, 1973.

5960 HISTOLOGIC FINDINGS OF THE PAROTID GLAND AND BICARBONATE CONTENT IN PAROTID SALIVA OF DOGS WITH EXPERIMENTALLY PRODUCED PANCREATITIS. *(E.)* Kakizaki, G.; Noto, N.; Fujiwara, Y.; Kato, E.; Ishidate, T.; Saito, T. (Akita Univ. Sch. Med., Japan). *Tohuku J. Exp. Med.* 108(2):165-177, 1972.

See also, 5953, 6073.

5961 WILSON'S DISEASE AND PREGNANCY. A CASE REPORT. *(E.)* Albukerk, J. N. (Southside Hosp. Lab., Bay Shore, N.Y.). *Fertil. Steril.* 24(6):494-497, 1973.

After her first pregnancy, a 21 yr old woman developed a tremor which was attributed to multiple sclerosis. During her second pregnancy, her neurologic signs regressed and remained improved until shortly after delivery of her second child. Each pregnancy resulted in a full-term healthy infant. After the second delivery, Wilson's disease was confirmed. On a low-copper diet and 1-2 gm penicillamine/day she remained well for 9 yr, during which time, at ages 31 and 36, she had 2 spontaneous abortions, each occurring during the 4th month of pregnancy. After the second abortion, she began taking her medication irregularly and died of bronchopneumonia. Autopsy revealed 8000 ml of ascites. The portal vein and its tributaries were occluded by recent thrombi. The liver weighed 1700 gm, was firm and cirrhotic. Fibrous bands of variable width delineated brown parenchymal nodules. Hepatocytes showed abundant lipofuscin pigment which disclosed minimal amounts of copper. There was no bile stasis, fatty change, or necrosis. Kidneys showed atrophy and dilatation of the convoluted tubules. Kayser-Fleisher rings were absent. The patient's improvement during pregnancy is attributed to the large amounts of copper uptake by the fetus and maternal elevation of ceruloplasmin which could have the same therapeutic end result as penicillamine treatment. The minimal amounts of copper in the liver biopsy and the disappearance of Kayser-Fleisher rings confirm the view that with prolonged cupriuresis and low-copper diet, maternal copper is depleted. It is suggested that copper deficiency resulting from long-term penicillamine therapy may have caused the spontaneous abortions.

5962 AUTOPSY FINDINGS IN A LONG-SURVIVING LIVER RECIPIENT. *(E.)* Starzl, T.; Porter, K. A.; Schroter, G.; Corman, J.; Groth, C. G.; Sharp, H. L. (Univ. Colorado Med. Ctr., Denver). *N. Engl. Med. J.* 289(2):82-84, 1973.

A 4-yr-old male received an orthotopic liver transplant from a 10-yr-old male donor. Rejections after 1 and 2 months were easily reversible. The highest bilirubin level was 6.1 mg/100 ml. Except for persistent transaminase increases from 50 to 200 IU, the patient was healthy with normal liver function at all times for the next 3½ yr. Immunosuppresive therapy consisted of cyclophosphamide or azathioprine (25 mg/day), prednisone (15 to 20 mg/day), and horse antilymphocyte globulin (1 injection/week). After 3 yr and 3 months, the patient was admitted with acute septicemia, (*Haemophilus influenzae*, type B) complicated by circulatory collapse, evidence of disseminated intravascular coagulation and acute deterioration of renal and hepatic function; SGOT peaked at 7700 IU and bilirubin at 21.9 mg/100 ml. Alkaline phosphatase rose 10 days later and prothrombin levels dropped to 25%. After improvement in renal function and prothrombin levels, the patient's condition deteriorated and he died 3 yr, 4 months, and 20 days after transplantation. Autopsy revealed extensive pneumonitis due to *pneumocystis carinii* and cytomegalovirus. In small scattered plumonary abscesses, branching hyphae of aspergillus were identified. Kidney, brain, lungs, and hepatic homograft all contained inclusion bodies typical of cytomegalovirus. A positive cytomegalovirus culture was obtained from the liver. Cholangiograms showed an essentially normal extrahepatic duct system with well visualized intrahepatic ramifications. Histological examination revealed almost complete occlusion of most of the small hepatic-artery branches and arterioles by massive intimal thickening. A number of vessels in the arteriogram were narrowed. Marked atrophy of the centrizonal hepatocytes in all lobules was seen, and small focal areas of necrosis of liver cells were present in some lobules. Cholestasis was marked with intracanalicular bile thrombi in the central parts of the lobules. Larger hepatic veins had no phlebosclerosis and these had free drainage into the vena cava and through the upper venous anastomosis. The gallbladder was ulcerated. It is almost certain that the sudden late deterioration of homograft function was a complication of the *Hemophilus* septicemia. It is suggested that vascular lesions in the liver resulted either from an antigen-antibody reaction in the vessel walls or from the deposition of immune complexes at this site.

5963 METABOLIC EFFECTS OF HEPATIC REPLACEMENT IN WILSON'S DISEASE. *(E.)* Groth, C. G.; Dubois, R. S.; Corman, J.; Gustafsson, A.; Iwatsuki, S.; Rodgerson, D. O.; Halgrimson, C. G.; Starzl, T. E. (Univ. Colorado Sch. Med., Denver). *Transplant Proc.* 5(1):829-833, 1973.

Liver transplants had been performed 3 and 1½ yr earlier for terminal hepatic failure and moderate cirrhosis plus severe neurologic involvement, resp. in 2 boys with Wilson's disease. In an 11 yr old, serum bilirubin was 20.6 mg/100 ml; serum albumin, 1.5 g/100 ml; prothrombin time, 13% of normal; and blood ammonia, 432 μg nitrogen/100 ml; serum albumin, serum bilirubin was 2.9 mg/100 ml; serum albumin, 2.9 g/100 ml; and prothrombin time, 44% of normal. To provide information on the role of the liver in Wilson's disease, studies were made of copper metabolism in these patients. Both patients had a high liver copper value but only the second boy had low ceruloplasmin, total serum copper, and increased urinary copper excretion. Biopsy specimen of the grafts showed copper levels that were normal or only slightly elevated. The serum and urine findings in the second patient normalized, his neurologic symptoms abated, and the Kayser-Fleischer rings became less prominent. These findings are consistent with the hypothesis that the metabolic defect in Wilson's disease is liver based.

5964 INTRAARTERIAL INFUSION IN THE TREATMENT OF LIVER METASTASES. *(Sp.)* D'Auria, A. E.;

Iriondo, L. S.; Priario, J. C. (no affil.). *Cir. Uruguay* 42(1):16-19, 1972.

Intraarterial infusions of 5-fluorouracil (250-1000 mg/day for total doses of 1250-11,500 mg) were administered to 13 patients, aged 29-67 yr, with liver metastases from primary tumors in the colon and rectum (6 patients), gallbladder (2), stomach (1), pancreas (1), and breast (1). Only 1 of these patients was jaundiced and 5 had ascites. In 3 cases, 5-fluorouracil was combined with procarbazine (65-250 mg/day for total doses of 375-1065 mg). Cytostatic agents were infused through a catheter introduced into the common hepatic artery via the gastroepiploic and gastroduodenal arteries; supraduodenal branches of the pyloric artery were routinely ligated to prevent the development of gastritis and, in 1 case, a prophylactic cholecystectomy was performed to prevent the development of chemical cholecystitis. Although none of these patients were cured, intraarterial infusion of 5-fluorouracil increased the mean survival time from 48 days (controls) to 259 days. Survival times ranged from 8 days to 3 yr and 2 months. Severe complications included intestinal obstruction (2 patients) and perforation of the gastroduodenal artery and a fistula in the duodenum which was the cause of death (1 patient); 6 less severe complications resulted from this procedure. Drug side effects included vomiting (2 cases), diarrhea (2 cases), and stomatitis, alopecia, glossitis, and gastritis (1 case each).

5965 TREATMENT OF HEPATIC COMA AND HEPATORENAL SYNDROME. *(E.)* Fischer, J. E.; James, J. H. (Massachusetts Gen. Hosp., Boston). *Am. J. Surg.* 123(2):222-230, 1972.

Certain manifestations of hepatic failure may be due to the accumulation of false neurochemical transmitters which act by replacing normal transmitters at nerve endings in peripheral and central nervous systems. Acute hepatic coma was produced in rats by a two stage ligation of hepatic vasculature within 24 hr. Octopamine increased in the brain as the severity of coma increased. Phenylethanolamine was elevated in brains of animals who appeared moribund. Increased amounts of brain octopamine in animals with shunts was achieved by p.o. administration of either phenylethylamine or phenylalanine. Similar elevation of brain and heart octopamine was achieved in normal animals with use of monoamine oxidase inhibitors. The urinary excretion of octopamine increased in human patients in hepatic coma, patients with liver disease without coma, and patients without obvious liver disease. A 43 yr old woman with Laennec's cirrhosis, hypersplenism, and active pancreatitis was admitted for bleeding from esophageal varices and a 57 yr old male alcoholic was admitted with gastrointestinal bleeding. When these 2 patients were in hepatic coma with cardiovascular abnormalities including high cardiac output, low peripheral resistance, and low urinary sodium with diminished urine volume they were treated with L-dopa administered (by gastric tube and nasogastric tube, resp.) in increasing amounts to 50 mg/kg in divided doses per 24 hr. This treatment resulted in diminished cardiac output, correction of cardiovascular abnormalities and awakening from hepatic coma. After L-dopa treatment was stopped, cardiac output again rose with rising venous pressure and decreasing blood pressure with a fall in urinary output. In 8 patients suffering from hepatorenal syndrome with normal blood volumes, high cardiac outputs, low peripheral resistance and low urinary sodium levels metaraminol administration was followed by increased peripheral vascular resistance, decreased cardiac output, and increased urinary sodium excretion. Metaraminol did not improve mental status as did L-dopa.

5966 INTRAHEPATIC SCLEROSING CHOLANGITIS ASSOCIATED WITH A FAMILIAL IMMUNODEFICIENCY SYNDROME. *(E.)* Record, C. O.; Eddleston, A. L. W. F.; Shilkin, K. B.; Williams, R. (King's Coll. Hosp. Med. Sch., London, England). *Lancet* (7819):18-20, 1973.

An unusual hepatic lesion occurred in an 18-year-old girl with an immunodeficiency syndrome. Family history revealed 2 of 4 family members had had hepatic abnormalities of a similar nature. Of these 4, 3 died from fulminating septicemia and the 4th from fulminant hepatitis. Symptoms in the present case included a 4-month history of right-upper-quadrant abdominal pain and diarrhea and steatorrhea with recurrent childhood asthma and eczema. Smallpox vaccination at age 17 resulted in widespread vesicular rash. Serum bilirubin was slightly raised, 2.0 mg/100 ml; alkaline phosphatase, 1440 IU/liter; IgG, 3200 mg/100 ml; IgA, 67 mg/100 ml; IgM, less than 10 mg/100 ml. These immunological abnormalities indicated a partial deficiency of both humoral and cellular immune systems. Histological examination of the liver showed thin fibrous bands linking portal tracts which contained a moderate infiltrate of lymphocytes and plasma cells, together with concentric fibrosis around the bile ducts. The lesions in this family resemble most closely intrahepatic sclerosing cholangitis. There was no evidence of ulcerative colitis, retroperitoneal fibrosis, or Reidel's thyroiditis.

5967 FINE STRUCTURE OF PRIMARY LIVER TUMORS AND TUMOR-BEARING LIVERS IN MAN. *(E.)* Ma, M. H.; Blackburn, C. R. B. (Roy. Prince Alfred Hosp., Sydney, Australia). *Cancer Res.* 33(7):1766-1774, 1973.

Electron microscopic studies were made of 5 hepatomas, 2 of which were present in noncirrhotic livers and 3 in patients with cirrhosis. Tumor cells were characterized by scantiness of subcellular organelles. Apart from the apparent deletion of peroxisomes, bile canaliculi, and very low-density lipoprotein particles in some tumors, ultrastructural alterations were otherwise nonspecific. On the other hand, the hepatocyte origin of 4 of the tumors was indicated by the occurrence in tumor cells of 1 or another organelle that characterizes the normal hepatocyte. Virus-like particles, 80 nm, were observed in 1 tumor. The unusual occurrence in some nonneoplastic hepatocytes of numerous microtubular inclusions in the endoplasmic reticulum cisternae is reported. The preponderance of these tubules in the cisternae of the smooth endoplasmic reticulum and adjacent rough endoplasmic reticulum suggests they may represent some metabolic products, possibly proteins, which are synthesized in the rough endoplasmic reticulum and transported to the smooth. Their possible relation to the malignant process is not understood.

5968 ASPECTS OF FRUCTOSE METABOLISM IN NORMAL MAN. *(E.)* Bergstrom, J.; Furst, R.; Gallyas, F.; Hultman, E.; Nilsson, L. H.; Roch-Norlund, A. E.; Vinnars, E. (St. Eriks Hosp., Stockholm, Sweden). *Acta Med. Scand.* (suppl 542): 57-64, 1972.

In 3 normal human subjects infusion of fructose (1 g/kg/hr, i.u.) for 4 hrs resulted in an increase in the glycogen content of the m. quadriceps femoris of 3.3 g/kg wet muscle (muscle samples obtained by needle biopsy). This was equal to the amount of glycogen formed after a glucose infusion of the same magnitude in 7 subjects. In muscle previously depleted of glycogen by exercise, infusion of glucose resulted in twice as much glucogen being formed, as did a fructose infusion. Formation of liver glycogen was much higher after fructose than after glucose infusion (liver samples obtained by Menghini biopsy). Studies by hepatic vein catheterization indicated that glucose formation by the liver was insufficient to account for the synthesis of muscle glycogen, which presumably occurred directly from fructose taken up by the muscle. The occurrence of high lactic acid concentrations in blood resulting from infusion of fructose could be partly abolished by simultaneous infusion of amino acids, thus lessening the risk of lactic acidosis.

5969 BEHAVIOR OF SOMATOTROPIC HORMONE SECRETION IN THE COURSE OF CHRONIC LIVER DISEASE. *(It.)* Giordano, G.; Marugo, M.; Minuto, F.; Barreca, T. (Sci. Inst., Intern. Med., Univ. Genoa, Italy). *Arch. E. Maragliano Patol. Clin.* 27(3/4): 175-193, 1971.

Serum levels of human growth hormone (HGH) were determined in 11 patients (10 men and 1 woman, aged 30-68 yr) with chronic liver disease before and at various intervals after i.v. infusion of 30 g arginine monohydrochloride, 0.1 IU/kg insulin, or 1 mg glucagon hydrochloride. Administration of insulin and arginine to patients with chronic liver disease increased serum HGH levels, which reached a maximum after 60 min; the values attained were in the upper normal range. Infusion of glucagon into patients with chronic liver disease produced less of a response in serum HGH levels than when the glucagon was infused into controls. Insulin produced extremely large variations in blood sugar levels: responses ranged from slight (3 patients) to normal (3 patients) to pronounced (2 patients). Although no correlation was observed between portal hypertension and changes in serum HGH levels, there was a certain relation between blood ammonia levels and basal serum HGH levels, i.e., hormone levels were higher in patients with blood ammonia levels of more than 100 μg/100 ml. A less pronounced inverse relation exists between blood protein levels and basal serum HGH levels. No correlation was found between clinical signs of cirrhotic hyperestrogenism (gynecomastia, palmar erythema, spider nevi, etc.) and increased response of HGH to various stimuli.

5970 HEPATOMA ASSOCIATED WITH MARKED PLASMACYTOSIS AND POLYCLONAL HYPERGAMMAGLOBULINEMIA. *(E.)* Fenoglio, C.; Ferenczy, A.; Isobe, T.; Osserman, E. F. (Columbia Presbyterian Med. Ctr., New York, N.Y.). *Am. J. Med.* 55(1):111-115, 1973.

A 63 yr old male patient had marked polyclonal hypergammaglobulinemia associated with micronodular cirrhosis and hepatoma. The patient had a history of limited use of alcohol all his adult life, and had no known episode of hepatitis or exposure to hepatotoxins. Marked elevation of immunoglobulin levels, particularly gamma globulin, appeared to be associated with the development of hepatic neoplasia. In addition to bone marrow plasmacytosis, plasma cells were associated with the regenerative cirrhotic and neoplastic hepatic nodules. The immunoglobulin and histopathologic findings suggest that the marked elevation of the gamma globulin levels are related to the neoplastic, rather than to the underlying cirrhotic, process. This case suggests that diffuser hypergammaglobulinemia and plasma cell hyperactivity may occur with hepatoma.

5971 BIOCHEMICAL STUDIES ON LIVER TUMORS OF CHILDREN. *(E.)* Murthy, A. S. K.; Vawter, G. F.; Kopito, L.; Rossen, E. (Children's Cancer Res. Fdn., Boston, Mass.). *Arch. Pathol.* 96(1):48-52, 1973.

Hepatic tumors of 8 children (6 girls and 2 boys, aged 4 months - 12.7 yr) were studied for the following: morphology, fetoprotein, histochemistry of enzymes, biochemistry, and mineral composition. In 7 cases the morphological classification of the tumor was hepatoblastoma; in the 8th, hepatocellular carcinoma. Livers of 8 children served as controls. Nucleic acid and protein content of the tumors appeared to be related to nucleocytoplasmic ratio and histologic maturity. There was a marked decrease in the zinc content of all tumors and a reduction in the activity of alkaline phosphatase and lactate dehydrogenase, both zinc-dependent enzymes. These enzymes could not be activated *in vitro* by addition of zinc salt, suggesting an altered metalloenzyme complex in these tumors. The differentiation of tumors may be correlated with fetoprotein. This protein was not demonstrable in 2 embryonal tumors. Fetal hepatoblastomas resembled livers of newborn children. No truly minimal deviation hepatoma was identified by the factors used in this study.

5972 OCCURRENCE OF LIVER-SPECIFIC ANTIGEN IN ADULT HUMAN SERUM. *(E.)* Smith, J. B.; Iverson, G. M. (U.S. Naval Hosp., Bethesda, Md.). *Clin. Exp. Immunol.* 13:209-212, 1973.

A liver-specific, water-soluble autoantigen (F-antigen) was detected by double diffusion using specifically prepared antiserum in 30 of 285 adult serum samples tested. F-antigen was found most frequently in disorders associated with hepatocellular destruction such as metastatic cancers (4 of 11 patients) and acute viral hepatitis (8 of 25). Of the latter patients, 14 had hepatitis associated with the transient presence of Australia antigen. F-antigen was also found in serum from patients with Laennec's cirrhosis (3 of 28), steatonecrosis (2 of 13), and hepatocellular carcinoma (2 of 11). F-antigen was not found in 25 chronic hepatitis cases, in the hepatic vein blood of 3 patients with alcoholic cirrhosis, or in 9 cases of hepatic regeneration. These results indicate that F-antigen appears in the serum when liver dysfunction is maximal and thus may have prognostic value. In 2 cases of acute viral hepatitis, F-antigen appeared at the peak of illness and disappeared from the serum as the hepatic enzymes fell.

5973 HYDRALAZINE DISEASE ASSOCIATED WITH TRANSIENT GRANULOMAS IN THE LIVER. A CASE REPORT. *(E.)* Jori, G. P.; Peschle, C. (Inst. Med. Pathol., Univ. Naples, Italy). *Gastroenterology* 4(2):1163-1167, 1973.

Hydralazine treatment (75 mg/day) was instituted in a 51 yr old woman whose blood pressure was 200/105. Therapy proved unsuccessful and 17 months later the dose was increased to 150 mg/day. After 1 month of this higher dosage, the patient complained of generalized aching and migratory arthralgias, resulting in low-grade fever associated with symmetrical swelling of the interphalangeal joints. Serum bilirubin was 0.7 mg/100 ml direct, serum alkalin phosphatase was 7.7 Bodansky U, BSP sodium retention was 7.0% at 45 min, and SGOT was 55 U/ml. Biopsy revealed many well-defined epithelioid granulomas scattered within an otherwise undisturbed parenchyma. Giant cells were present in about 1/4 of these granulomas. Hydralazine was replaced with reserpine and a thiazide diuretic. The patient was also given prednisone (20 mg/day). Within weeks she was entirely asymptomatic, except for mild arthralgia. Rechallenge with hydralazine was not permitted, but the clinical and histological evidence indicates that hydralazine caused a granulomatous hepatitis in the course of hydralazine disease.

5974 ANAESTHESIA IN THE PRESENCE OF LIVER DISEASE AND FOR HEPATIC TRANSPLANTATION. *(E.)* Farman, J. V. (Addenbrooke's Hosp., Cambridge, England). *Br. J. Anaesth.* 44(9):946-52, 1972.

Aspects of severe liver disease of concern to the anesthetist are described. These are portal hypertension, hepatocellular failure, circulatory changes, ascites, effects of hepatic detoxification of drugs, clotting factors, abnormalities of protein synthesis, reduced cholinesterase production and cerebral effects of liver failure. Physiological and biochemical monitoring in major hepatic surgery is necessary to prepare the anesthetist for unexpected events. The operation of liver transplantation is outlined. This procedure demonstrates the effects of nonperfusion of the liver as well as those of the anhepatic period. While plasma glucose levels are surprisingly little affected, changes in potassium level and acid-base state are quite severe and need careful management. The inferior vena cava is occluded temporarily, giving rise to profound circulatory changes. In the postoperative period the patients show a metabolic alkalosis with hypoglycemia and hypokalemia, and there is a risk of underventilation.

5975 FOCAL NODULAR HYPERPLASIA OF THE LIVER. ANGIOGRAPHY AND RADIOISOTOPE SCANNING. *(E.)* McLoughlin, M. J.; Colapinto, R. F.; Gilday, D. L.; Hobbs, B. B.; Korobkin, M. T.; McDonald, P.; Phillips, M. J. (Toronto Gen. Hosp., Canada). *Radiology* 107:257-263, 1973.

Angiographic findings are described for focal nodular hyperplasia of the liver in 3 women (aged 18-32 yr) and in a 9 yr old girl. A total of 7 lesions were found, 6 of which were small, well circumscribed and highly vascular with prolonged diffuse contrast staining. All of the small lesions were strikingly similar and occurred in the 3 older females. The 4th case had a solitary lesion which was supplied by enlarged hepatic artery branches, contained a mass of abnormal, tortuous, irregular vessels and caused a dense, well-defined tumor stain. The displacement of feeding arteries in the patient with the large area of focal nodular hyperplasia and in liver cell adenomas may reflect the slow growth of these lesions and portend a benign rather than a malignant process. An absence of invasiveness is also indicated by the well-defined margins of both focal nodular hyperplasia and adenomas during the capillary phase. It is suggested that the presence of capsular arteries in liver cell adenoma may be the differentiating characteristic between that lesion and focal nodular hyperplasia. It is also noted that the uptake of colloidal radioisotopes may help in the diagnosis of focal nodular hyperplasia, since areas of focal nodular hyperplasia contain reticuloendothelial cells while most mass lesions of the liver do not.

5976 PATHOGENESIS OF CHANGES IN THE HEPATO-BILIARY SYSTEM IN WORKERS EMPLOYED IN THE PLASTICS INDUSTRY. *(Rus.)* Reneva, T. G.; Aver'ianova, O. S. (Med. Inst., Sverdlovsk, USSR). *Gig. Tr. Prof. Zab.* (6):28-30, 1972.

A study of male and female workers in a Sverdlovsk plastics factory showed that the prevalence of hepatobiliary disease increased significantly with the duration of employment at this factory. Since the ratio of affected males to females was 1:5 among workers exposed to plastics and 1:9 among unexposed controls, some factor in the work environment, common for both men and women, affects the prevalence of hepatobiliary disease. Clinical examinations, performed on 126 plastics workers with hepatobiliary disease, showed that the dominant symptom was a pain syndrome associated, in 69 patients, with dyspepsia. Biliary inflammation, manifested by increased body temperature and duodenal findings, was present in 76.4% of the workers; plastics biliary dyskinesia was present in 62% of the plastics workers but in only 39.5% of the controls; hepatomegaly was detected in 33 patients (26.2%). Disturbances in liver function, which were detected in a large percentage of the plastics workers, never occurred without biliary involvement. Disturbances in liver function were associated, in many cases, with manifestations of hypothalamic disorders. None of the workers had symptoms of primary toxic hepatitis. It is suggested that hypothalamic irritation, caused by chemical agents, leads to biliary dyskinesia which, in turn, results in secondary inflammation of the intrahepatic bile ducts. Sedative therapy (minor tranquilizers, barbiturates, bromides, etc.), combined with spasmolytic and cholinergic agents, is recommended. Biliary inflammation should be treated with antibiotics, biliary drainage, and desensitization to prevent development of hepatitis.

5977 BENIGN MESENCHYMAL TUMOR (ANGIOFIBROMA) OF THE LIVER ASSOCIATED WITH HYPOGLYCEMIA. *(Ger.)* Gmunder, U.; Schmid, M. (Med. Clin., Univ. Zurich, Switzerland). *Acta Hepatogastroenterol.* 19(6):425-430, 1972.

5978 LIVER BIOPSY AND THE DIAGNOSIS OF MALARIA. *(Dan.)* Beck, H. (Munic. Hosp., Copenhagen, Denmark). *Ugeskr. Laeger* 134(32):1665-1667, 1972.

5979 INTRAPERITONEAL RUPTURE OF A MALIGNANT HEPATOMA (HEMATIC PSEUDOCYST). SUBSEGMENTAL LIVER RESECTION. *(Fr.)* Combe, J.; Aubert, D.; Ranfaing, J.; Ledoux, A.; Gillet, M. (no affil.). *Lyon Chir.* 68(4):308-310, 1972.

5980 CLASSIFICATION OF ACUTE AND CHRONIC LIVER DISEASES. *(E.)* Schmidt, E.; Schmidt, F. W. (Hannover Med. Sch., Germany). *Scand. J. Gastroenterol. (Suppl.)* 8(19):13-35, 1973.

5981 THERAPEUTIC ACTION OF A PREPARATION CONTAINING TOTAL LIVER EXTRACT, CYANOCOBALAMINE, AND AMINO ACIDS FROM THE KREBS CYCLE IN ACUTE AND CHRONIC LIVER DISEASE. *(It.)* Pignattari, S.; Sarti, F.; Toscano, S.; Dal Monte, P. R. (Inst. Med. Semeiotics, Univ. Bologna, Italy). *Minerva Med.* 63(53):2861-2872, 1972.

5982 A CASE OF LATE SYPHILLIS OF THE LIVER. *(Pol.)* Lao, A.; Minich, R.; Skowron, S. (Helena Wolf Hosp., Lodz, Poland). *Wiad. Lek.* 25(19):1779-1781, 1972.

5983 SHOULD OVULATION INHIBITORS ALSO BE USED FOR PATIENTS WITH LIVER DISEASE? *(Ger.)* Runnebaum, B. (Clin. Obstet. Gynecol., Univ. Heidelberg, Germany). *Munch. Med. Wochenschr.* 114(21):1036-1038, 1972.

5984 THE LIVER IN CONGESTIVE HEART FAILURE: A REVIEW. *(E.)* Dunn, G. D.; Hayes, P.; Breen, K. J.; Schenker, S. (Vanderbilt Univ. Sch. Med., Nashville, Tenn.). *Am. J. Med. Sci.* 265(3):174-189, 1973.

5985 PRIMARY CANCER OF THE LIVER. *(Fr.)* Sankale, M. (Fac. Med., Dakar, Senegal). *Progr. Med.* 100(6):221-225, 1972.

See also, 5533, 5657, 5659, 5723, 5724, 5745, 5748, 5754, 5757, 5758, 5759, 5777, 5790, 5795, 5798, 5834, 5888, 5919, 5997, 6001, 6081, 6098.

LIVER AND BILIARY TRACT

Hyperbilirubinemic States

5986 HEPATIC BILIRUBIN GLUCURONIDATION IN GILBERT'S SYNDROME. *(E.)* Felsher, B. F.; Craig, J. R.; Carpio, N. (Univ. Southern California Sch. Med., Los Angeles). *J. Lab. Clin. Med.* 81(6):829-837, 1973.

Hepatic bilirubin uridine diphosphate-glucuronyl transferase and β-glucuronidase were assayed in liver biopsies from normal subjects, 16 patients with Gilbert's syndrome (14 males and 2 females), and 37 patients with acute viral hepatitis. In the

Gilbert's syndrome group uridine diphosphate-glucuronyl ransferase was uniformly reduced, unrelated to the erum bilirubin concentration, unaffected by acute hanges in caloric intake, and not significantly al- ered by phenobarbital administration (400 mg/day). n the hepatitis group, uridine diphosphate-glucuronyl ransferase was normal and significantly increased y phenobarbital ($p < 0.001$). Neither a serum nor epatic inhibitor of uridine diphosphate-glucuronyl ransferase was detectable in patients with Gilbert's yndrome. β-glucuronidase activity was normal in oth groups of patients, and in the hepatitis group t was not increased by phenobarbital. Although artial impairment of hepatic bilirubin glucuronida- ion is the hallmark of Gilbert's syndrome, addition- l factors, such as acute caloric withdrawal, parti- ipate in the manifestation of unconjugated hyper- ilirubinemia.

987 JAUNDICE IN PREGNANCY: A FOLLOW-UP STUDY OF THE SERIES OF WOMEN ORIGINALLY REPORTED Y L. THORLING. I. THE PREGNANCIES. *(E.)* Furhoff, . K.; Hellstrom, K. (Serafimer Hosp., Stockholm, weden). *Acta Med. Scand.* 193(4):259-266, 1973.

o characterize all pregnancies in a group of women o had been jaundiced during at least one pregnancy nd to investigate the possible existence of predis- osing and precipitating factors to itching and jaun- ice during pregnancy, a follow-up was conducted in l patients diagnosed about 20 yr earlier as having aundice or viral hepatitis in early or late preg- ancy. The women were characterized with regard to ecurrence, and type and course of symptoms during all eir pregnancies. It was found that the criteria of re- urrent cholestasis of pregnancy were fulfilled in 16 ases, such cases having experienced pruritus with or thout jaundice during all their pregnancies. Further- ore, almost 50% of these 16 women had close relatives o experienced pruritus, often associated with jaundice ring pregnancy. There was no evidence of exposure viral hepatitis at the time of the pregnancies. correlation was established between the presence hypertension and/or proteinuria and the presence severity of jaundice and pruritus. Drug consump- on, biliary tract disease and preeclampsia in gen- al did not appear to have precipitated jaundice or ruritus in any group of women. Bacterial infections y have precipitated jaundice or pruritus in 5 omen. Of possible factors related to the etiology cholestasis of pregnancy, the most suggestive s, therefore, hereditary predisposition. The ture of conditions responsible for non-recurrent undice with or without itching in pregnant women mains obscure.

88 TANNING FROM PHOTOTHERAPY FOR NEONATAL JAUNDICE. *(E.)* Woody, N. C.; Brodkey, J. (Tulane Med. Sch., New Orleans, La.). *J ediatr.* 82(6):1042-1043, 1973.

undice was detected in a full-term 20 hr old black girl when serum bilirubin concentration was 11.2 mg%. Phototherapy was begun and she was treated for 6 of every 8 hr for 5 days until serum bilirubin concentrations reached 8.3 mg%. Tanning was observed in this infant and was probably due to immediate pigment darkening followed by melanogenesis that occurred because the phototubes had a comparatively strong energy emission at 400-600 nm., the Plexiglas screen permitted these wavelengths to pass, and the infant had some preformed melanin in her skin.

5989 EFFECT ON NEONATAL JAUNDICE OF OESTROGENS AND PROGESTOGENS TAKEN BEFORE AND AFTER CONCEPTION. *(E.)* McConnell, J. B.; Glasgow, J. F. T.; McNair, R. (Roy. Maternity Hosp., Belfast, Northern Ireland). *Br. Med. J.* 3(5881): 605-607, 1973.

5990 CLINICAL PROBLEM: FAMILIAL CHOLESTATIC JAUNDICE IN PREGNANCY. *(Fr.)* Brechot, C. (no affil.). *Bull. Mem. Soc. Med. Paris* 176(2): 41-46, 1973.

5991 EFFECT OF SEASONAL CHANGES IN THE INCIDENCE OF NEONATAL JAUNDICE. *(It.)* Dansi, A.; Kehyayan, E. (Provincial Specialized Hosp., Milan, Italy). *Minerva Pediatr.* 25(8):350-352, 1973.

5992 USE OF PHENOBARBITAL TO TREAT HYPERBILIRUBINEMIA IN NEWBORNS. *(It.)* Vazzoler, G.; Forabosco, A.; Muz, G. (Munic. Hosp., Pordenone, Italy). *Minerva Pediatr.* 24(22):925-927, 1972.

5993 INTRAHEPATIC CHOLESTASIS CAUSED BY DANANTHIZOLE. *(Sp.)* Kravetz, D. (A. Posadas Polyclin., Haedo, Argentina). *Rev. Esp. Enferm. Apar. Dig.* 38(6):725-738, 1972.

See also, 5644, 5781.

Nonviral Hepatitis and Hepatic Injury

5994 HEPATORENAL TOXICITY FOLLOWING FLUROXENE ANESTHESIA. *(E.)* Tucker, W. K.; Munson, E. S.; Holaday, D. A.; Fiserova-Bergerova, V.; Turner, B. M. (Univ. Florida Coll. Med., Gainesville). *Anesthesiology* 39(1):104-107, 1973.

A 47-year-old female was admitted for lumbar laminectomy for treatment of back pain. No history of jaundice, renal disease, or alcoholic intake was noted. An overdosage of an unknown depressant drug had been consumed 5 months prior to admission in a suicide attempt. Medication prior to anesthesia included atropine (0.6 mg), meperidine (50 mg), and diazepam (10 mg). Anesthesia itself was induced with thiopental (300 mg) and maintained with nitrous oxide (60%) and fluroxene at inflow concentration of 3% or less. The patient was under the anesthetic for 5 1/3 hr. On the first postoperative day her temperature spiked, and nausea and vomiting developed. By day 3 mental confusion had developed. On day 4 total bilirubin was 10.1 mg/100 ml; SGOT was 1,320 units. Day 5 saw the development of hemorrhagic disorders. Necropsy and histologic examination revealed evidence of an acute toxic process active in the liver. The total fluorine, trifluoroethanol, and trifluoroacetic acid contents of the blood and urine were similar to those values in 9 patients surviving fluroxene anesthesia without incident. The liver content of total fluorine was within the normal range. However, adipose tissue contained about twice the expected fluoride ion concentration. In this case, it is postulated that prior exposure to other drugs caused induction of microsomal enzymes before the introduction of fluroxene. It is possible that enzyme induction may influence the occurrence of a toxic metabolite. It is also possible that conditions favoring one metabolic pathway over another, or an unusual production of trifluoroethanol or some other metabolites, were responsible for this patient's hepatic necrosis.

5995 FATAL HEPATIC NECROSIS IN A WOMAN RECEIVING CHEMOPROPHYLAXIS WITH ISONIAZID. *(E.)* Bailey, W. C.; Thompson, D. H.; Carson, B.; Greenberg, H. B. (Dept. Health, New Orleans, La.). *Am. J. Gastroenterol.* 59(6):512-517, 1973.

Fulminant massive necrotic hepatitis caused the death of a 38-year old, tuberculin-positive, elementary school, cafeteria worker, 19 weeks after she had started chemoprophylaxis with isoniazid (300 mg/day). Anorexia, weight loss, weakness, increased fatigability, and dark urine caused her to seek medical help 30 days after starting isoniazid therapy. Her symptoms had developed insidiously, other signs of drug reaction being absent, and she had continued at her work until 10 days before her death in hepatic coma. On admission, laboratory tests showed bilirubin 27.7 mg/100 ml, SGOT 860 U; and LDH 980 U. Her sclerae were bright yellow, and her abdomen was diffusely tender and distended; pitting edema involved the skin on her face, abdominal wall, and all four extremities. Prothrombin time was 60 sec. After examination of her clinical and pathological findings and after a thorough epidemiologic investigation failed to disclose any history of exposure to viral hepatitis, it was concluded that the patient had died of isoniazid-associated liver disease.

5996 INAPPARENT ACUTE ALCOHOLIC HEPATITIS. *(Sp.)* Iturriaga, H.; Ugarte, G.; Altschiller, H.; Insunza, I. (San Borja Hosp., Santiago, Chile). *Rev. Med. Chile* 100(1):9-13, 1972.

On the basis of liver biopsy findings, 320 men, hospitalized for treatment of alcoholism and with no manifest signs of liver disease, were divided into 3 groups: (1) 36 with acute alcoholic hepatitis, (2) 15 with cirrhosis but not alcoholic hepatitis, and (3) 112 with moderate to severe fatty liver. Histological, clinical, and laboratory findings were compared for groups (1), (2), and 29 randomly selected patients from group (3) with uncomplicated fatty liver. The overall prevalence of cirrhosis, including that associated with alcoholic hepatitis, was 10.3% (33 cases). The age of patients was similar in all 3 groups, while the history of alcoholism was slightly longer in alcoholic hepatitis and the quantity of alcohol ingested over the past year was significantly greater in cirrhosis. Of the 36 patients with alcoholic hepatitis, 35 had fatty liver and 18 had cirrhosis. Fibrosis was present in 77% of patients with alcoholic hepatitis and no evidence of cirrhosis, suggesting that alcoholic hepatitis may be a percursor of cirrhosis. Extracellular acidophilic antibodies of the Councilman type were detected in 21 patients with alcoholic hepatitis; only 1 patient had central hyaline sclerosis. Only 1 of 15 cirrhotics displayed marked signs of collapse; all 15 had fatty liver. Fibrosis was present in 8 of the 29 patients with fatty liver. Hepatomegaly was detected in all 15 cirrhotics, in 86.2% of those with uncomplicated fatty liver, and in 80.5% of those with alcoholic hepatitis. Serum bilirubin levels above 1.2 mg/100 ml were significantly more common in cirrhosis and alcoholic hepatitis than in uncomplicated fatty liver. Prothrombin levels below 70% of normal were significantly more common in cirrhosis than in fatty liver, and the percentage of positive flocculation tests was significantly higher in cirrhosis than in the other 2 groups. The percentage of patients with elevated SGOT levels was significantly higher in alcoholic hepatitis than in the other groups, but there was no significant difference between mean SGOT levels for these 3 groups.

5997 LIVER DISEASE IN KIDNEY TRANSPLANT PATIENTS RECEIVING AZATHIOPRINE. *(E.)* Ireland, P.; Rashid, A.; von Lichtenberg, F.; Cavallo, T.; Merrill, J. P. (Bernalillo County Med. Ctr., Albuquerque, N. M.). *Arch. Intern. Med.* 132(1):29-37, 1973.

The liver disease in 24 kidney transplant patients (14 males and 10 females, aged 11-52 yr) receiving azathioprine was reviewed to determine the cause and appropriate management. Azathioprine hepatotoxicity could not be implicated in any of the 24 patients. There was no correlation between the course of the liver disease and azathioprine administration and withdrawal. Nonspecific reactive hepatitis occurred in 7 patients and was associated with sepsis and other complications; viral hepatitis occurred in 12, based on the clinical course, histopathologic and laboratory findings, and tests for Australia antigen; and in 5 patients the cause of the liver disease could not be determined. The high morbidity of viral hepatitis in these patients (fulminant hepatitis in 1 and postnecrotic cirrhosis in 2) suggested an adverse effect of immunosuppression. Liver disease is not an indication to discontinue azathioprine therapy, but rather to reduce total immunosuppression whenever posible.

5998 LIVER STRUCTURE AND FUNCTION FOLLOWING SMALL BOWEL RESECTION. *(E.)* Gupta, M. C.; Neale, G.; Dowling, R. H. (Roy. Postgrad. Med. Sch., London, England). *Gut* 14(6):438-443, 1973.

The observation that 6 patients (3 men and 3 women, aged 37-76 yr) with extensive small bowel resection have impaired hepatocellular function with reduced BSP clearance and fatty change in biopsies from the liver led to a systematic study of liver structure and function following proximal and distal small bowel resection in the male Wistar rats. While anesthesia and surgery impaired BSP clearance *per se*, small bowel resection further reduced BSP clearance with impairment of both uptake and excretion phases of BSP excretion. The increased BSP retention was more marked after distal than after proximal small bowel resection, but in both experimental groups the abnormalities of BSP excretion spontaneously returned o normal 3-4 weeks after surgery. Circulating liver enzymes were normal but serum alkaline phosphaase was significantly depressed, particularly after istal resection. The changes in rat serum alkaline hosphatase may be due to removal of the intestinal rush border isoenzyme in small bowel resection. soenzyme studies showed that the depression of serum alkaline phosphatase was due to a reduced intestinal soenzyme. While serum levels remained consistently epressed up to 8 weeks after proximal resection, erum alkaline phosphatase returned to normal 2-4 eeks after ileectomy. Serum AP levels appear closey related to alkaline phosphatase concentrations in he upper small intestine and may provide an indirect arker of intestinal mucosal regeneration following leal resection in the rat. Light microscopy reealed no morphological differences in the secions of the liver obtained from resected animals ompared with controls. No fatty infiltration of epatocytes or inflammatory cell infiltration was oted. While these minor changes in hepatic strucure and function would normally be of little clinial importance, the additional insult of hepatic dysunction may well be important in malnourished paients after extensive small bowel resection.

5999 HALOTHANE HEPATITIS. *(E.)* Qizilbash, A. H. (Dept. Pathol., McMaster Univ., Hamilton, Ontario, Canada). *Can. Med. Assoc. J.* 108:171-177, 1973.

Hepatocellular injury following halothane anesthesia occurred in 5 patients (4 women and 1 man, aged 20-64 yr), of whom 4 had multiple exposures to the anesthetic. Of the 5, 3 died from submassive to massive liver cell necrosis. The 2 survivors developed jaundice and/or dark urine following each exposure to halothane; liver biopsy in 1 showed centrilobular and linear areas of necrosis. Fever, anorexia, nausea, vomiting, abdominal pain, and jaundice were present in all cases. In the 2 survivors the prothrombin time was less than 20 sec throughout the course of the disease, whereas in the 3 who died the prothrombin time was more than 20 sec from the onset. Halothane should not be administered to patients who require several operations within a short period of time, or to those who develop fever and jaundice after drug exposure. Maximum total serum bilirubin was 3.3 and 11.8 mg/100 ml in the survivors and 22.3-38.4 mg/100 ml in the 3 who died. Maximum SGOT values were 1080 and 1800 U in the survivors and 1320, 2160, and 2320 U in the other 3 cases.

6000 ISONIAZID ADMINISTRATION AND LIVER INJURY. *(E.)* Rudoy, R.; Stuemky, J.; Poley, J. R. (Children's Mem. Hosp., Oklahoma City). *Am. J. Dis. Child.* 125(5):733-736, 1973.

A 6 yr old Caucasian boy was treated for active tuberculosis with isoniazid (20 mg/kg/day), p-aminosalicylic acid (300 mg/kg/day), and streptomycin (10 mg/kg/day). After 4 weeks of therapy he was readmitted with high fever, a morbilliform exanthem, peripheral eosinophilia, enlargement of the liver, nausea, vomiting, upper abdomenal pain, and abnormal test results. Serum alkaline phosphatase was 58 King-Armstrong U; SGOT, 156 Reitman-Frankel U; and total serum bilirubin, 0.5 mg/100 ml. All symptoms disappeared upon withdrawal of isoniazid and p-aminosalicylic acid, but they reappeared upon isoniazid challenge. The liver lesions showed changes similar to those in hepatitis. There was no cholestasis. The histologic appearance of the liver lesion and the clinical manifestations suggested a hypersensitivity reaction, probably of the delayed type. The fact that this child was given twice the recommended dosage for his age may indicate the reaction to isoniazid is dose-related.

6001 LIVER BIOPSY IN PSORIASIS. A CONTROLLED STUDY. *(E.)* Zachariae, H.; Sogaard, H. (Marselisborg Hosp., Aarhus, Denmark). *Dermatologica* 146(3):149-155, 1973.

Liver biopsies were performed on 79 patients (44 males and 35 females, average age 54 yr), with severe psoriasis; 40 were being treated with methotrexate at the time. Biopsies were also taken from 60 control patients (39 males and 21 females, average age 61 yr), 18 of whom were patients with Parkinson's disease and 42 were victims of sudden death. Methotrexate (i.m. or p.o.) was given at doses of 20-25 mg initially; these were reduced to 15 mg when the psoriasis was controlled. The average duration of treatment was 24 months. In a number of cases, treatment was intermittent. Steatosis, periportal inflammation, and focal necrosis were all present with significantly greater frequency among psoriatics than among controls. Pathological liver changes also were greater in the psoriatic group. There were no differences in steatosis or fibrosis between the psoriatics treated with methotrexate and those not so treated. It is suggested that, besides the influence of obesity, exposure to methotrexate, and alcohol intake, psoriasis itself, or factors precipitating the outbreak of skin symptoms, may contribute to liver pathology in this disease.

6002 NONSPECIFIC MESENCHYMAL REACTION AND PARENCHYMAL DAMAGE OF THE LIVER IN PATIENTS WITH HODGKIN'S DISEASE. *(Ger.)* Oehlert, W.; Dischler, W. (Pathol. Inst., Univ. Freiburg, Germany). *Dtsch. Med. Wochenschr.* 97(9):323-327, 1972.

Liver involvement, proven by laparoscopy and biopsy, was found in 24 of 161 patients with Hodgkin's disease in various clinical stages and different histological forms. In the remaining 116 patients a mesenchymal reaction of differing severity was demonstrated, ranging from diffuse activation of the reticuloendothelial system grade (1) to histiocytic granulomas grade (2) with demonstration of eosinophilic granulocytes and atypical reticulum cells grade (3). There was no positive correlation between the incidence or severity of the mesenchymal reaction and certain histological forms of Hodgkin's disease. With increasing involvement of lymph nodes the incidence and severity of mesenchymal reactions increased. In all 24 patients with liver involvement the mesenchymal reaction was grade 3. It is not yet clear whether grade 3 mesenchymal reaction is a forerunner of Hodgkin's infiltration or a non-specific reaction.

6003 DISTURBED HEPATIC FUNCTION DURING ISONIAZID CHEMOPROPHYLAXIS. MONITORING THE HEPATIC FUNCTION OF 427 HOSPITAL EMPLOYEES RECEIVING ISONIAZID CHEMOPROPHYLAXIS FOR TUBERCULOSIS. *(E.)* Bailey, W. C.; Taylor, S. L.; Dascomb, H. E.; Greenberg, H. B.; Ziskind, M. M. (Charity Hosp., New Orleans, La.). *Am. Rev. Resp. Dis.* 107:523-529, 1973.

Elevations of SGOT developed in 37 of 427 hospital employees receiving isoniazid chemoprophylaxis (300 mg of isoniazid and 50 mg of vitamin B_6 daily) for 4 to 8 months. Isoniazid was discontinued in 5 patients because they also had symptomatic hepatitis and in 8 asymptomatic employees because they also had abnormal serum values of total bilirubin or alkaline phosphatase or both. In 24 subjects, however, SGOT elevations were the only indications of hepatic injury. Testing their hepatic function biweekly or monthly enabled evaluation of criteria based on SGOT limits for interrupting their chemoprophylaxis. Treatment with isoniazid was stopped whenever the SGOT exceeded 100 U on 2 occasions, or whenever SGOT exceeded 250 U on 1 occasion. As a result, isoniazid was stopped in 5 subjects with elevations of SGOT. It was continued in 19 others, who remained asymptomatic; their tests after completion of chemoprophylaxis showed normal values for SGOT. In this population, monitoring the hepatic function tests provided an additional margin of safety, particularly for the black male employees, who had the highest frequency of abnormalities of SGOT during chemoprophylaxis. Since isoniazid chemoprophylaxis offers the best means for eradicating tuberculosis in the United States, it is recommended that any practicable measures be adopted that might increase its safety and, thereby, its scope.

6004 AN UNUSUAL CASE OF LEPTOSPIROSIS. *(E.)* Parry, W. H.; Seymour, M. W. (Public Health Office, Nottingham, England). *Practitioner* 210(1260):791-793, 1973.

A 47 yr old male, hospitalized with jaundice, was in a state of severe dehydration secondary to severe vomiting. He and his pet dog had been bitten by 2 guard dogs 18 days earlier. The patient had received 0.5 ml tetanus toxoid 2 days before admission to the hospital. Alkaline phosphatase was 105 IU; total bilirubin was 9.4 mg/100 ml. Agglutination tests showed trace agglutination antibodies to *Leptospira icterohaemorrhagiae* and *L. canicola* at 1:1000. On further study a diagnosis of leptospirosis was made. Mobile leptospira was found in the urine of the pet dog. There was a large, rat-infested area near the patient's home and it is felt that infected urine from rats caused the initial infection in the patient's pet. The patient, in caring for the wounds of his animal, was in turn infected in the cuts he had received from the guard dogs. A second infected dog was found in the same household and it was suggested that both dogs be destroyed. This report illustrates the need for rodent control in areas of heavy infestation and strict surveillance of pet and guard dogs by veterinarians.

6005 CHRONIC HELOTHANE EXPOSURE: LIVER DAMAGE IN ANESTHETISTS. *(Ger.)* Grimmeisen, H. (Bad Tolz Hosp., Germany). *Anaesthesist* 22(2): 41-46, 1973.

6006 POTENTIATION BY PREVIOUS DRUG THERAPY OF HEPATOXICITY FOLLOWING PARACETAMOL OVERDOSAGE. *(E.)* Wright, N.; Prescott, L. F. (Roy. Infirm., Edinburgh, Scotland). *Scot. Med. J.* 18:56-58, 1973.

6007 POSSIBLE ACUTE LIVER TOXICITY FROM THE HYPOLIPIDEMIC AGENT 1-METHYL-4-PIPERIDYL-BIS(P-CHLOROPHENOXY)-ACETATE. *(E.)* Bochner, F.; Cham, B. E.; Eadie, M. J.; Hooper, W. D.; Knowles, B. R.; Sutherland, J. M.; Tyrer, J. H. (Roy. Brisbane Hosp., Herston, Australia). *Toxicol. Appl. harmacol.* 24(4):653-656, 1973.

See also, 5993.

LIVER AND BILIARY TRACT

Acute Viral Hepatitis

008 RACE AND RISK OF HEPATITIS IN NARCOTIC ADDICTS. *(E.)* Whaley, W. H.; Galambos, . T. (Grady Mem. Hosp., Atlanta, Ga.). *Am. J. ig. Dis.* 18(5):460-466, 1973.

group of 393 unselected heroin addicts (67% nder 25 yr, 76% males, and 63% black) who participated voluntarily in a methadone withdrawal rogram were studied during a 1-yr period. There as a higher frequency of hepatitis, HBA-g positive, nd SGOT measurement over 250 U among white than mong black addicts, but no sex difference was etected. HBAg was positive in 68 patients; 42 of hese had hepatitis and 24 of the 26 asymptomatic BAg-postive addicts developed hepatitis. After BAg-positive illness, second attacks of hepatitis n 6 cases were all HBAg-negative. It is suggested hat the tendency to share the same needle results n increased frequency of HBAg+ hepatitis among oung addicts and that infection of nonneedle-using snorters" may result from sexual transmission of BAg.

009 HERPES SIMPLEX INFECTIONS DURING HEPATITIS. *(It.)* Albanese, M.; Barba, G.; Brancato, .; Bruno, F.; Di Cuonzo, G. (Inst. Hyg., Univ. alermo, Italy). *Riforma Med.* 86(13):487-489, 1972.

14-yr-old boy was hospitalized 10 days after he ad developed a high fever, severe headache, and ersistent vomiting and 7 days after appearance of morbilliform rash; pronounced jaundice and a recomatose state developed 1 day before hospitalization. In addition to jaundice, the following ere observed on admission: coated tongue, haryngitis, mild hepatomegaly, temporal and spatial disorientation, slow reaction of pupils o light, and muscular hypertonia with exaggeration f osteotendinous reflexes. Laboratory findings ncluded elevated SGOT and SGPT activities and yperbilirubinemia (22 mg/100 ml total). After days of precoma and psychomotor agitation, the oy began to improve. Increased cerebrospinal luid pressure was relieved by a spinal tap. SGOT, GPT, and bilirubin levels returned to normal, and the patient was discharged after 30 days. A strain of *Herpes simplex* virus was isolated from a throat culture inoculated intracerebrally into newborn mice. Suspensions of infected mouse brain were then inoculated into continuous monkey kidney and primary rabbit kidney cell cultures. Inoculation of this virus into scarified rabbit cornea induced keratitis followed by encephalitis. The virus was neutralized by standard antiserum for *Herpes simplex.* Serum samples taken from the patient on admission and after 30 and 60 days had antibody titers of 1:10, 1:40, and 1:640, resp. It is hypothesized that symptoms referable to the nervous system and liver were produced by localization of herpes virus in these two areas. The relatively mild symptoms in this case differ markedly from the usually severe symptoms of primary herpes infections when they occur in symptomatic form.

6010 COMPARISON OF THE DIAGNOSTIC VALUE OF THE ACTIVITIES OF SERUM FRUCTOSE DIPHOSPHATE ALDOLASE AND LIVER-SPECIFIC ALDOLASE IN VIRAL HEPATITIS. *(Rus.)* Zavelishko, A. F. (Benderskaia Repub. Hosp., USSR). *Zdravookhr. Ross. Fed.* (3):20-23, 1972.

Fructose monophosphate (liver-specific) aldolase and nonspecific aldolase activities were determined simultaneously in serum from 57 patients with viral (40 with infectious and 19 with serum) hepatitis. The patient group consisted of 33 women, 22 men, and 3 children with mild (18) and moderately severe (39) forms of hepatitis. In patients with acute viral hepatitis the mean value for fructose monophosphate aldolase was 17-23 times higher than that in normal controls, whereas the mean nonspecific aldolase activity was only 6-6.4 times higher in hepatitis patients than in controls. This difference in liver-specific and nonspecific aldolase activities gradually decreased as the patients began to recover. Elevated fructose monophosphate aldolase activities persisted longer than elevated nonspecific aldolase activities. Prior to discharge from the hospital, bilirubin values had normalized in all 57 patients, but 21 still had some direct bilirubin in their serum, 10 had increased nonspecific aldolase activity, and 52 had increased liver-specific aldolase activity. It is recommended that fructose monophosphate aldolase activities, because of their greater sensitivity, be used as the criterion for recovery from viral hepatitis rather than nonspecific aldolase activities.

6011 SERUM AUTOANTIBODIES IN HEPATITIS ASSOCIATED ANTIGEN (HAA) POSITIVE PATIENTS. A POSSIBLE INDEX OF CELL-MEDIATED IMMUNITY TO THE ASSOCIATED-INFECTIVE AGENT.

(E.) Dudley, F. J.; O'Shea, M. J.; Sherlock, S. (Roy. Free Hosp., London, England). *Clin. Exp. Immunol.* 13:367-372, 1973.

Sera from 134 HAA positive patients have been studied for the presence of a variety of autoantibodies. The patients were divided into groups dependent on the clinicopathological severity of the associated liver disease. The group of 134 patients included patients with acute hepatitis (52), chronic aggressive hepatitis or active cirrhosis (35), chronic persistent hepatitis (23), asymptomatic carriers of HAA with no biochemical evidence of liver disease (15), and primary liver cell carcinoma with underlying cirrhosis with variable degrees of liver cell failure (9). Both smooth muscle antibody and rheumatoid factor were found in all groups of patients. However, their incidence and titer was higher in the groups of patients who had clinical and pathological evidence of the more active liver cell damage. As autoantibodies in viral infections may be an index of the presence of cell mediated immunity to the causative infective agent, these results could support the hypothesis that cell mediated immunity is important in the pathogenesis of liver cell damage in HAA positive patients. It is hypothesized that production of acute hepatitis depends upon the normal response of thymus-derived lymphocytes (T cells) to antigens associated with viral hepatitis. Impairment of this immunity is related both to persistence of the infective agent and continuing liver damage, while absence of specific T cell immunity is related to persistence of the antigen without continuing liver cell damage.

6012 SUBTYPES OF AUSTRALIA ANTIGEN AMONG PATIENTS AND HEALTHY CARRIERS IN COPENHAGEN. A RELATION BETWEEN THE SUBTYPES AND THE DEGREE OF LIVER DAMAGE IN ACUTE VIRAL HEPATITIS.

(E.) Nielsen, J. O.; Le Bouvier, G. L.; (Blegdam Hosp., Copenhagen, Denmark). *N. Engl. J. Med.* 288(24):1257-1261, 1973.

The D(ad +, y-) and Y(ay +, d-) subtypes of Australia antigen were determined in 199 antigen-positive patients with various liver diseases and 23 healthy carriers. In 183 consecutive patients with biopsy-verified acute viral hepatitis, the antigen was the Y subtype in 79% and the D subtype in 21%. A similar subtype distribution was found in 22 patients with biopsy-verified chronic hepatitis and persistent antigenemia. In contrast, all 10 patients with cirrhosis and all the healthy carriers had antigen of the D subtype. A striking epidemiologic difference was found, in that 98% of the 107 drug addicts had the Y subtype, while the D subtype predominated in the 36 "sporadic" cases, i.e., those without any known contact with patients with hepatitis and without any known inoculation or visits to specific countries. The acute disease in the 183 patients with acute hepatitis was more severe in the group of patients with antigen of the D subtype, as judged by both histologic and biochemical criteria. Thus, the different subtypes of Australia antigen are associated with particular epidemiologic and clinical features of these acute hepatitis cases.

6013 THE ROLE OF CARRIERS OF VIRAL HEPATITIS IN THE EPIDEMIOLOGY OF THIS DISEASE.

(Rus.) Iarovoi, P. I. (no affil.). *Zdravookhr. Ross. Fed.* (3):6-10, 1972.

An epidemiological study was made of 388 patients with viral hepatitis from 308 foci of infection in Kiev: 69.9% were under 17 yr old; 58.5% were males and 41.5% were females. In 101 cases (26.0%) the source of infection was a patient in the acute stage of viral hepatitis and in 62 cases (15.9%) a patient who had recovered from the disease. The incidence of viral hepatitis was highest in winter and spring, particularly among preschool and school children. This is apparently because children who contracted the infection in October and November returned home from the hospital and served as a source of infection for their families and classmates and because diagnostic, immunological, and prophylactic procedures which cause injury to the skin are generally performed in September and October. Epidemiological evidence indicates that 51.2% of patients who had clinically recovered from viral hepatitis continued to be a public health hazard for the first 3 months of their convalescence: 39% served as sources of infection for 3-6 months, 6.1% for 7-9 months, and 3.7% for 10-12 months after their discharge from the hospital. Infection was transmitted more often by the parenteral than by the enteral route. Serum aldolase, SGOT, and SGPT determinations made on patients who had recovered from viral hepatitis showed that the largest percentage of subjects with increased serum enzyme activities was found in the spring, perhaps because these subjects had spring vitamin deficiencies, as a result of which blood vessel permeability increases and the penetration of enzymes from liver to bloodstream rises. The percentage of subjects with increased serum enzyme activities is inversely proportional to the time elapsed since the patients' discharge from the hospital. It is suggested that 20-30% of patients who have recovered from viral hepatitis have a subclinical form which gradually clears up over a period of 3-6 months or more.

6014 INTRINSIC INTERFERENCE CAUSED BY HEPATITIS SERA.

(E.) Berthold, H.; Mielke, G.; Merk,

W. (Inst. Hyg., Univ. Freiburg, Germany). *Proc. Soc. Exp. Biol. Med.* 143(3):698-700, 1973.

Australia (Au)-antigen-positive and Au antigen-negative sera were obtained during the acute phase of hepatitis. A tissue culture of human diploid fibroblast cells from embryonic lungs developed intrinsic interference when infected with hepatitis sera. Hemadsorption-negative plaques appeared following Herts Newcastle disease virus challenge on day 12 after infection with hepatitis sera. By day 20 after infection, large hemadsorption-negative areas were often found. Intrinsic interference was induced by Au-antigen (Au)-positive as well as by Au-antigen-negative hepatitis sera. Of the 39 samples taken, 28 produced typical plaques, 13 of which were Au-antigen-positive and 15 were Au-antigen-negative. Thus it was demonstrated in sera from patients with acute hepatitis (both Au-antigen-positive and-negative) agents which are infectious for human tissue culture and which can be passaged in them. These agents were not neutralized by γ-globulin nor by a hemophiliac serum containing Au antibodies when attempts were made to neutralize the virus in the initial serum taken from hepatitis patients.

6015 THE SIGNIFICANCE OF CYTOMEGALIC INCLUSION VIRUS IN LIVER DISEASE IN CHILDREN. *(Ger.)* Peller, P.; Goetz, O. (Pediatr. Clin. Univ. Munich, Germany). *Dtsch. Med. Wochenschr.* 97(9):321-323, 1972.

Complement-fixing antibody titers against cytomegalic inclusion virus were measured in 113 children, aged 0-17 yr, with liver disease. These included 76 with hepatomegaly of unknown etiology, 31 with acute or chronic hepatitis, 3 with neonatal hepatitis, and 3 with postperfusion syndrome or serum hepatitis; 410 age-matched children with no evidence of liver disease served as controls. A titer of 1:8 or higher was detected in 41 patients (36%) but in only 45 (11%) of the controls. The incidence of these antibodies was the same in all age groups. Cytomegalic inclusion virus was isolated from the urine of 12 of the 48 patients tested. These patients consisted of 8 with hepatomegaly, 2 with giant cell hepatitis, 1 with serum hepatitis, and 1 with postperfusion syndrome after heart surgery. Only 2 of the 90 controls excreted the virus in their urine. These findings suggest that cytomegalic inclusion virus may be a serious disease for growing children and adults, as well as for the fetus and newborns.

6016 ATTEMPTS TO DETECT HEPATITIS B VIRUS BY NEGATIVE HEMADSORPTION ASSAY. *(E.)* Vorndam, A. V.; Murphy, B. L.; Hollinger, F. B.; Maynard, J. E. (Baylor Coll. Med., Houston, Tex.). *Proc. Soc. Exp. Biol. Med.* 143(2):396-399, 1973.

Evaluations were made of 23 sera containing hepatitis B antigen (HB Ag). Some areas of nonhemadsorbing cells were found in 17 specimens at some stage during the incubation period in human embryonic lung fibroblasts or in WI-38 cells, a human diploid cell strain. Different types of negative hemadsorption patterns were observed. The most frequent type consisted of small plaques of 20-30 cells with discrete margins surrounded by apparently healthy cells. These plaques were scattered randomly throughout the monolayer, and ranged from 0 to 5 in number per tube. They were observed both in cultures inoculated with HB Ag and in cultures inoculated with diluent alone. A second pattern was larger, up to $1\ \text{mm}^2$, with irregular margins and appeared to follow the growth pattern of the cells in the monolayer. This pattern was seen most often in cultures inoculated with HB Ag-positive serum, but sometimes also was observed in HB Ag-negative serum and diluent controls. A third type was thought to be due to a metabolic abnormality or nutritional deficiency of the cells. Problems in this assay system include nonreproducible results, difficulties in determining when a specimen is positive, the large number of operations to perform in the assay itself, and the inexplicable "positive" results observed in presumably normal human sera as well as in cell control tubes inoculated with diluent only. It is concluded that the negative hemadsorption test is not specific for the agent of type B viral hepatitis.

6017 SPREAD OF ACUTE TYPE-B HEPATITIS IN LONDON. *(E.)* Heathcote, J.; Sherlock, S. (Roy. Free Hosp., London, England). *Lancet* (7818):1468-1470, 1973.

Acute type-B hepatitis was studied in 67 patients (43 male and 27 female, aged 10-62 yr) to determine the source of the hepatitis-B antigen (HBAg) infection. Of 162 contacts of 51 of the patients, 154 submitted blood samples and the serum was tested for HBAg. Only 16 patients had parenteral exposure to HBAg in the 6 months prior to their becoming ill. Of the remaining 51 patients, 13 had had sexual contact (2 were male homosexuals) and another 12 (4 were male homosexuals) had had nonsexual contact with individuals who were either jaundiced of HBAg positive. Of 8 HBAg-positive carriers who were traced, 5 were apparently healthy carriers. Two other patients probably had similar contacts. In the remaining 24 patients, no definite source of infection was identified, but 9 of the 20 males in this group were either homo- or bisexual. Of the whole group, sexual or domestic contact was the definite or most likely source of infection in 27 (40%) of the patients.

6018 HEPATITIS B ANTIGENS: SEPARATION OF TWO POPULATIONS DIFFERING IN PARTICLE SIZE DISTRIBUTION. *(E.)* Neurath, A. R.; Cosio, L.; Prince, A. M.; Lippin, A.; Ikram, H. (New York Blood Ctr., N.Y.). *Proc. Soc. Exp. Biol. Med.* 143(2):440-445, 1973.

In a new fractionation procedure applied to sera containing hepatitis B antigen (HBAg), 42 nm diameter spherical particles, together with 20 nm wide tubular forms were concentrated and separated from most of the smaller 20 nm diameter spherical particles and serum proteins by a simple method. The addition of polyethylene glycol 6000 to HBAg-containing serum precipitated the 42 nm spherical and 20 nm tubular particles and left most of the 20 nm spherical particles in the supernatant. Supernatants contained 70 to 97% of the HBAg originally present. Rate zonal sedimentation of supernatant fluids and of the redissolved precipitates obtained from the same serum showed considerable differences in the size distribution of HBAg specific particles present in the 2 preparations. Further experimentation showed that the sedimentation rates of HBAg in each preparation were related to their distinct morphologic features and not to the formation of aggregates in the precipitates. Decreasing the concentration of polyethylene glycol below 5.5% did not increase the selectivity of precipitation but did diminish the proportion of HBAg recovered in the precipitate. It was felt that the partial separation by precipitation with polyethylene glycol of the distinct morphological forms of HBAg will facilitate their further purification and characterization.

6019 AUSTRALIA ANTIGEN AND ANTIBODY AMONG PATIENTS ATTENDING A CLINIC FOR SEXUALLY TRANSMITTED DISEASES. *(E.)* Fulford, K. W. M.; Dane, D. S.; Catterall, R. D.; Woof, R.; Denning, J. V. (Middlesex Hosp. Med. Sch., London, England). *Lancet* (7818):1470-1473, 1973.

Serum samples from 974 patients attending a clinic for sexually transmitted diseases were tested for Australian antigen (HBAg) and its antibody (HBAb). Of these patients, 17 were HBAg positive and 47 were HBAb positive; the remaining 910 patients had neither antigen nor antibody detectable by immunodiffusion. A preponderance of HBAg-positive patients came from Mediterranean and Middle Eastern countries; the HBAb-positive patients were predominantly of British origin. Both HBAg and HBAb groups contained a significant percentage of single men. There was no significant difference based on social class or occupation. The HBAb group had a high frequency of syphilis and gonorrhea in their histories. Patients with HBAg had a similar high frequency of gonorrhea, but none had a history of syphilis. A greater incidence of viral and fungal infections had occurred in the HBAg group; these infections were mostly of genital herpes, genital warts, and monilial balanitis. The HBAb group had more homosexuals and patients with 3 or more sexual contacts in the preceding 6-month period. None of the 47 patients with HBAb were known to have used condoms or occlusive caps. Male homosexuals appeared 7 times as likely to have antibody as male heterosexuals. It is suggested that in the United Kingdom hepatitis type-B virus is commonly transmitted by the sexual route.

6020 SPONTANEOUS HEPATOBRONCHIAL COMMUNICATIONS PRECEDING PYOTHORAX IN A PATIENT WITH SUSPECTED LIVER ABSCESS. A CASE REPORT. *(E.)* Okuda, K.; Kanda, Y.; Fukuyama, Y.; Sumikoshi, T. (Chiba Univ. Hosp.; Japan). *Gastroenterology* 65(1):124-129, 1973.

Transhepatic cholangiography for suspected biliary tract disease demonstrated communications between the right liver and the lung in a 34 yr old/diabetic male who presented with malaise, hepatomegaly, and a productive cough. Purulent pleuritis developed after several weeks. An insidious cryptogenic liver abscess caused the occurrence of hepatopulmonary fistulae before pleuropulmonary complications became evident. It was inferred that pyogenic changes in the liver parenchyma altered the intrahepatic lymphatics in an early phase of the disease, and subsequent formation of cephalad lymphatic channels through the so-called "bare area" of the diaphragm explained the pleuropulmonary complication that is common in liver abscess.

6021 AUSTRALIA ANTIGEN IN THE MOTHERS OF PREMATURE INFANTS AND NEWBORNS WITH PERINATAL DISTURBANCES. *(Ger.)* Hower, J.; Luboldt, W.; Bohlmann, J. G. : Eckert, G. (Essen Clin., Ruhr Univ., Bochum, Germany). *Klin. Paediatr.* 184(4):272-275, 1972.

The transmission of Australia antigen was investigated in 102 mothers and 139 of their infants with perinatal disorders. All of these infants were separated from their mothers immediately after birth. Of these infants, 77 were premature, 44 had erythroblastosis due to ABO or Rh incompability, 8 had hyperbilirubinemia of unknown etiology, and 10 had other unspecified perinatal disorders. Australia antigen was found in serum from 2 women with no history of hepatitis and normal serum transaminase values. During observation periods of 113 days and 29 days, resp., neither infant had Australia antigen or symptoms of hepatitis.

6022 GEOGRAPHICAL VARIATION OF THE "W" SUBTYPE OF AUSTRALIA ANTIGEN. *(E.)* Mazzur, S.; Falker, D.; Blumberg, B. S. (Inst. Cancer Res., Philadelphia, Pa.). *Nature* [*New Biol.*] 243(123): 44-51, 1973.

6023 IS HEPATITIS CAUSED BY VIROIDS? *(E.)* Zuckerman, A. J. (London Sch. Hyg. Trop. Med., England). *Lancet* (7818):1486-1487, 1973.

6024 HEPATITIS IN THE AGED. *(E.)* Gibinski, K.; Fojt, E.; Suchan, L. (Silesian Sch. Med., Katowice, Poland). *Digestion* 8(3):254-260, 1973.

6025 HEPATITIS AFTER TATTOOING: A FATAL CASE. *(E.)* Hopkins, G. B.; Gostling, J. V. T.; Hill, I.; McNab, D. J. N.; Mullan, D. P.; Scutt, R. W. B.; Wright, E. A. (Health Clin. Wimborne, England). *Br. Med. J.* 3(5873):210-211, 1973.

26 HEPATITIS-ASSOCIATED (AUSTRALIA) ANTIGEN IN NIGERIANS. AN ULTRASTRUCTURAL STUDY.
.) Williams, A. O.; Almeida, J. D. (Univ. Coll.
sp., Univ. Ibadan, Nigeria). *Am. J. Trop. Med.*
g. 21(4):473-481, 1972.

27 STUDY OF VIRAL HEPATITIS IN THE HOSPITAL ENVIRONMENT: 40 CASES. *(Fr.)* Bertrand,
L.; Trepo, C.; Cosentino, C.; Brette, R.
ntiquaille Hosp., Lyon, France). *Lyon Med.*
7(2):139-145, 1972.

28 DIFFERENTIATION BETWEEN ACUTE ALCOHOLIC HEPATITIS AND ACUTE INFECTIOUS (VIRAL)
PATITIS. *(E.)* Fong, W.; Tan, K. K.; Tye, C. Y.
ept. Med., Univ. Singapore). *Am. J. Gastroenterol.*
(3):221-226, 1973.

29 AUSTRALIA ANTIGEN IN CHILDREN TREATED IN A HOSPITAL. *(Pol.)* Korczowski, R.
rovincial Hosp., Rzeszow, Poland). *Pediatr. Pol.*
(7):849-855, 1972.

30 VIRAL HEPATITIS AMONG HEALTH SERVICE WORKERS. *(Pol.)* Gajda, A.; Imielinska,
; Kozakiewicz, H. (Acad. Med., Gdansk, Poland).
. Tyg. Lek. 27(36):1398-1401, 1972.

6031 THROMBOHEMORRHAGIC SYNDROME IN PATIENTS WITH VIRAL HEPATITIS. *(Rus.)* Pateiuk, V. G.; Kuznik, B. N. (Chita Med. Inst., USSR). *Klin. Med.* 50(8):115-121, 1972.

6032 CARRIERS OF HEPATITIS ASSOCIATED ANTIGEN (HAA) IN GREECE. *(Gr.)* Kourea-Kremastinou, T.; Papevangelou, G. (Dept. Hyg. Epidemiol., Univ. Athens, Greece). *Acta Microbiol. Hellenica* 17(2):99-108, 1972.

6033 CONVERSION TO POSITIVITY OF FALSE NEGATIVE LATEX/HEPATITIS ASSOCIATED ANTIGEN AGGLUTINATION TEST UPON TREATMENT OF SERA WITH EDTA OR TRYPSIN. *(E.)* Spano, C.; La Licata, R. (Inst. Hyg. Univ. Palermo, Italy). *Z. Immunitaetsforsch.* 144(4):396-399, 1972.

See also, 5755, 5756, 5762, 5763, 5766, 5786, 5794, 5972, 6064.

LIVER AND BILIARY TRACT

Chronic Hepatitis

4 IMMUNOLOGIC STUDIES IN PATIENTS WITH CHRONIC ACTIVE HEPATITIS AND PRIMARY BILIARY CIRRHO-
. I. CYTOTOXIC ACTIVITY AND BINDING OF SERA TO
AN LIVER CELLS GROWN IN TISSUE CULTURE. *(E.)*
onetto, F.; Gerber, M.; Vernace, S. J. (Mount Sinai
. Med., City Univ., New York, N.Y.). *Proc. Soc.*
. Biol. Med. 143(3):756-760, 1973.

a was collected from patients with chronic liver
eases. Using the indirect fluorescent technique,
ibody from sera of 13 patients with chronic active
atitis or 7 patients with primary biliary cirrho-
, but not normal sera, bound to cells derived from
an liver biopsies. Weak, diffuse, and sometimes
nular staining of the cytoplasm of unfixed cells
ulted from incubation of sera containing mitochon-
al antibodies. Smooth muscle antibodies bound to
cultured cells in a filamentous pattern. When
a of patients with antibodies to smooth muscle,
ochondria, nuclei and hepatitis B antigen, as well as sera containing hepatitis B antigen, were applied to microwells containing liver cells, cytotoxic activity was not detected. Sera of 4 patients with chronic active hepatitis containing antibodies to smooth muscle and nuclei were incubated 2 days with autologous cell lines derived from liver biopsies. In no instance could morphologic alteration or reduction in the number of cells be detected. When cell lines other than liver cells were used as targets, e.g., human fibroblasts or human conjuctiva, cytotoxic activity could not be detected.

6035 ELECTROENCEPHALOGRAPHIC CHANGES IN CHRONIC HEPATITIS. *(E.)* Sowa, J.; Gatarski, J. (Med. Acad., Cracow, Poland). *Epidemiol. Rev.* 26(3): 299-303, 1972.

6036 THE CHARACTERISTICS OF THE WALDENSTROM FORM OF CHRONIC HEPATITIS. *(Fr.)*

Buligesco, L. (Hosp. Fundeni, Bucharest, Rumania). *Acta Gastroenterol. Belg.* 36(4-5):249-259, 1973.

6037 INDICATIONS FOR AND ADMINISTRATION OF IMMUNOSUPPRESSIVE THERAPY FOR CHRONIC HEPATITIS. *(Ger.)* Paumgartner, G. (Inst. Clin. Pharmacol., Univ. Bern, Switzerland). *Schweiz. Med. Wochenschr.* 103(5):158-161, 1973.

6038 CHRONIC ACTIVE HEPATITIS. *(E.)* Waldron, C. W. (Tucson Clin., Ariz.). *Ariz. Med.* 29(1):36-39, 1972.

See also, 5724, 5750, 5752, 5753, 5755, 5761, 5765.

LIVER AND BILIARY TRACT

Alcoholic Liver Disease

6039 ETHANOL AND METHANOL METABOLITES IN ALCOHOL WITHDRAWAL. *(E.)* Magrinat, G.; Dolan, J. P.; Biddy, R. L.; Miller, L. D.; Korol, B. (St. Louis VA Hosp., Mo.). *Nature (Lond.)* 244(5413):234-235, 1973.

Alcohol withdrawal was studied in 21 subjects (20 males and 1 female, aged 27-72 yr). The subjects were divided into two groups on the basis of initial blood ethanol levels: a low-alcohol group with ethanol levels less than 100 mg/100 ml and a high-alcohol group with ethanol levels well over 100 mg/100 ml. All patients received chlordiazepoxide, flurazepam, and a high potency vitamin B complex and C in a fixed schedule. Mean admission levels of other substances in the blood were as follows for the high-alcohol and low-alcohol groups, resp.: ethanol, 309 mg/100 ml vs 14.4 mg/100 ml; acetaldehyde, 0.747 vs 0.378 mg/100 ml; and methanol, 1.54 vs 0.17 mg/100 ml. Blood ethanol values for both groups returned to nonalcoholic levels during the 5 withdrawal days. However, blood acetaldehyde concentrations remained significantly higher in the high-alcohol group and formaldehyde-formic acid blood concentrations were significantly increased by day 3 (5.58 vs 1.20 mg/100 ml). The high acetaldehyde levels implicate the impurities contained in the alcoholic beverages consumed by these patients when "on the street." The delayed and marked elevation in blood concentrations of the methanol metabolites, formaldehyde-formate, supports the hypothesis that oxidative enzyme systems induced by chronic alcohol consumption will shift to metabolize methanol when ethanol is abruptly withdrawn. Initially, both groups had high total scores in ratings for withdrawal symptom intensity; subsequent ratings showed a rapid return to normal in the low-alcohol group. The only significant behavioral differences between the two groups occurred in sleeping and eating.

6040 BLOOD FLOW LIMITATIONS IN INTERPRETING MICHAELIS CONSTANTS FOR ETHANOL OXIDATION IN VIVO. *(E.)* Dedrick, R. L.; Forrester, D. D. (Natl. Inst. Hlth., Bethesda, Md.). *Biochem. Pharmacol.* 22:1133-1140, 1973.

A 2-compartment model permitting localization of biochemical parameters and consideration of blood flow between compartments is used to simulate the concentration of ethanol in the blood as a function of time. Comparison of model simulations with published data from rats indicates that the apparent Michaelis constants determined for rats by considering their ethanol concentration uniform in a single compartment are artifactual and highly dependent on hepatic blood flow. The effect of changing the hepatic blood flow over the reported range shows that purely physiologic effects such as regional perfusion can have a significant effect on observed rates of oxidation *in vivo*. This becomes particularly significant if the hepatic blood flow rate is altered by ethanol. A satisfactory Michaelis constant *in vivo* based on localization of the activity in the liver is within the range reported for liver ADH *in vitro*. To elucidate all major aspects of ethanol distribution and metabolism *in vivo*, a more sophisticated model is needed.

6041 PLASMA ARYLSULFATASE AND β-GLUCURONIDASE IN ACUTE ALCOHOLISM. *(E.)* Geokas, M. C.; Rinderknecht, H. (Sch. Med., Univ. California, Los Angeles). *Clin. Chim. Acta* 46(1):27-32, 1973.

Arylsulfatase activity in plasma of 57 chronic alcoholics (aged 25-46 yr) with acute alcoholic intoxication as 126 pmoles 4-methylumbelliferone sulfate (MUS) /min/ml plasma, compared with 52 pmoles MUS/min/ml plasma recorded for 56 normal subjects (aged 18-32 yr). β-glucuronidase activities in alcoholics and controls were 2330 and 510 µg phenophthalein/hr/100 ml plasma, resp. Arylsulfatase assays conducted on patients with Crohn's disease and various nongastrointestinal diseases in which the leukocyte count is abnormal did not reveal elevated levels of enzyme activities. It is felt that the elevated arylsulfatase activity in alcoholics does not reflect leukocyte arylsulfatase and probably originates in the liver, kidney, pancreas, or other organs. The simultaneous increase of arylsulfatase and β-glucuronidase activities in plasma of alcoholics suggest that alcohol affects the structural integrity and permeability of the cell membrane proper and of the intracellular membranes of various tissues, effecting the release of these hydrolases into the blood.

042 MALLORY BODIES IN LIVER BIOPSIES FROM CHRONIC ALCOHOLICS: A COMPARATIVE MORPHOLOGICAL, BIOCHEMICAL, AND CLINICAL STUDY OF TWO GROUPS OF CHRONIC ALCOHOLICS WITH AND WITHOUT MALLORY BODIES.

E.) Christoffersen, P.; Eghoje, K.; Juhl, E. (Kommunehospital, Copenhagen, Denmark). *Scand. J. Gastroenterol.* 31(3):341-346, 1973.

study was made of liver biopsies taken from 39 chro-ic alcoholics with, and 285 without, Mallory bodies. ll patients had a history of consuming more than 50 /day of ethanol for a period of longer than 1 yr; ost had histories longer than 20 yr. The majority n both groups drank beer, but the percentage of atients in the Mallory body group who also drank arder types of alcohol (59%) was significantly reater than that of similar patients in the group ithout Mallory bodies (32%). Histological studies ndicated that there was a significantly greater in-idence of fatty change, lipogranulomas, parenchymal nflammation, bile duct proliferation, and "portal" nglammation in the group with Mallory bodies. There as no observable differences in the incidence of fo-al liver cell necrosis, acidophilic bodies, lipofuscin, holestasis, or siderosis. Laboratory test values for he group with Mallory bodies versus the group without ere: alkaline phosphatase, 88.9 versus 75.5 U/liter; erum bilirubin, 1.7 versus 0.8 mg/100 ml; serum as-artate transaminase, 109.8 versus 59.3 U/liter; pro-hrombin-proconvertin, 76 versus 91% of normal; and SP retention, 19 versus 9% after 45 min. The only ymptom occurring with greater frequency in the allory bodies group was hepatomegaly. There have een no results which indicate that the presence of ertain changes induced formation of Mallory bodies. ather the results support the simultaneous occurrence, nd thus an etiological connection is suggested.

043 CHANGES IN IMMUNOGLOBULIN IgA AND TRANSFERRIN IN ALCOHOLIC LIVER DISEASE.

Sp.) de Prado Isla, L. H.; Artiga, L. (Jose de an Martin Clin. Hosp., Buenos Aires, Argentina). *rensa Med. Argent.* 59(22):835-840, 1972.

erum immunoglobulin (Ig) A and transferrin determinations were made on 28 chronic alcoholics (all men, aged 32-79 yr) with fatty liver (12 patients), alcoholic hepatitis (2), and portal cirrhosis (14) confirmed by liver biopsy. IgA levels were significantly increased (mean of 345 ± 34 mg/100 ml) in patients with fatty liver; still further increases, which paralleled the severity of the disease, were observed in patients with cirrhosis. Alcoholic liver disease was associated with a decrease in serum transferrin which also paralleled the severity of the disease (mean of 225 ± 21 mg/100 in fatty liver and 170 ± 10 mg/100 ml in cirrhosis). It is recommended that serum IgA and transferrin levels be used in place of liver biopsies to follow the development of alcoholic liver disease. Progression toward cirrhosis should be suspected when the ratio of IgA/transferrin is greater than 1.6.

6044 SENSORI-NEURAL HEARING LOSS IN ALCOHOLIC CIRRHOSIS.

(E.) Koff, R. S.; Oliai, A.; Sparks, R. W. (Boston VA Hosp., Mass.). *Digestion* 8(3):248-253, 1973.

Pure-tone audiological examinations were performed in 22 neomycin-treated and untreated stable male patients with alcoholic cirrhosis, 10 of whom had previously undergone portacaval shunt surgery. Of the 12 non-shunted patients (aged 37-56 yr), 3 had received neomycin (4 g/day for 1-5 weeks); of the 10 shunted patients (aged 41-60 yr), 4 had received neomycin (4-8 g/day for 2-4 weeks). Severe sensorineural hearing losses were found in the shunted group only, regardless of whether or not they had previously received neomycin. Normal audiograms were seen only among non-shunted cirrhotics. Air conduction hearing thresholds for frequencies above kilohertz were significantly higher (poorer hearing) in the shunted than in the non-shunted group. Thresholds were also significantly higher in shunted patients who had not received neomycin than in non-shunted untreated cirrhotics. These results indicate that factors other than neomycin may contribute to hearing loss encountered in patients with alcoholic cirrhosis.

6045 THE INFLAMMATORY STEATONECROSIS OF THE ALCOHOLIC LIVER. PERSONAL EXPERIENCE AND REVIEW OF THE LITERATURE.

(Fr.) De Vos, M.; Roels, H.; Demeulenaere, L. (St. Andre Clin., Tielt, Belgium). *Acta Gastroenterol. Belg.* 36(4-5):239-248, 1973.

6046 SERUM PROTEINS OF HEPATIC AND EXTRAHEPATIC ORIGIN IN ALCOHOLIC CIRRHOSIS.

(E.) Marasini, B.; Agostoni, A.; Stabilini, R.; Dioguardi, N. (Inst. Med. Path., Univ. Milan, Italy). *Clin. Chim. Acta* 40(2):501-502, 1972.

See also, 5633, 5634, 5635, 5643, 5653, 5655, 5660, 5822, 6028, 6040.

Cirrhosis

6047 AN ASSESSMENT OF THE VALIDITY OF PREOPERATIVE HEMODYNAMIC STUDIES IN PORTAL HYPERTENSION.

(E.) Smith, G. W. (Baltimore City Hosp., Md.). *Surgery* 74(1):130-138, 1973.

Preoperative hemodynamic studies were performed, followed by the intraoperative assessment of portal blood flow, in 64 patients with portal hypertension resulting from postsinusoidal outflow obstruction. Three hemodynamic stages have been defined, based upon the hepatic artery:portal vein flow ratio measured in 18 patients. Results afford statistical support to justify defining the same hemodynamic stages on the basis of maximum perfusion pressure, which was measured in 60 patients. The preoperative hemodynamic tests were the estimated hepatic blood flow (58 patients), corrected wedged hepatic vein pressure (43), hepatic venous oxygen saturation (38), splenic pulp pressure (33), degree of portal-systemic shunting (37), diminished portal flow velocity (32), and splenic uptake of colloid on a scan (24). Only the corrected wedged hepatic vein pressure showed a significant correlation when statistically correlated with the intraoperative hemodynamic stage. Most preoperative hemodynamic studies seem to bear no statistical significance to actual portal blood flow; their value must be questioned in the assessment of cirrhotic patients with portal hypertension.

6048 MALLORY BODIES IN A CASE OF PRIMARY BILIARY CIRRHOSIS: AN ULTRASTRUCTURAL AND MORPHOGENETIC STUDY.

(E.) Monroe, S.; French, S. W.; Zamboni, L. (Harbor Gen. Hosp., Torrance, Calif.). *Am. J. Clin. Pathol.* 59(2):254-262, 1973.

An ultrastructural study was made of Mallory bodies observed in a percutaneous liver biopsy of a 70 yr old female with biliary cirrhosis. Light microscopic examination of sections revealed prominent cellular alterations in the peripheral hepatic plate, mostly in the form of deposition of hyaline material over extensive regions of the cytoplasm. From morphological and staining characteristics the formations were identified as Mallory bodies. Electron microscopic examination of thin sections stained with lead citrate showed that small and medium sized Mallory bodies were consistently associated with ribosomes, mostly arranged in a cochleariform configuration, which were either in the inclusions or distributed at their periphery. The topographic relation between the ribosomes and filamentous material of the Mallory bodies was always very close, and overlapping of the 2 elements was frequently noted, particularly in the small inclusions. The number of ribosomes in and around the inclusions decreased with the increase in size of the Mallory bodies. This suggests that the material of the Mallory body matrix may be produced by the synthetic activity ribosomes. Also, ribosomal clusters were in close association with mitochondria characterized by interrupted outer and inner membranes, the individual ribosomes apparently being continuous with the matrix and cristae of the mitochondria through the multiple interruptions along the mitochondrial membranes. This suggests further that the ribosomes involved in the synthesis and deposition of Mallory body material are of mitochondrial origin and that they are liberated into the adjacent cytoplasm following disassembly of portions of the mitochondrial membranes. Thus, it would seem that the mitochondrial are equipped for the synthesis of extramitochondrial substances.

6049 EFFECT OF 3,4-DIHYDROXYPHENYLALANINE (LEVODOPA) IN HEPATIC COMA.

(Sp.) Gonzalez-Posada, J.; Hernandez-Peniche, J.; Tirado-Arroyave, S. (no affil.). *Arch. Invest. Med.* 3(1): 1-6, 1972.

In addition to drugs administered to decrease blood ammonia levels and restore water and electrolyte balance, L-dopa (1500 mg/day through a nasogastric tube) was given to 10 randomly selected patients (7 men and 3 women, aged 42-74 yr) with hepatic coma between stages III and IV. In 7 patients the clinical diagnosis was cirrhosis, probably caused by alcohol and malnutrition, and portal hypertension; 1 patient had a tentative diagnosis of postnecrotic cirrhosis and in 2 cases the etiology was unknown. The coma was precipitated by bronchopneumonia (2 cases), recent acute alcoholic intoxication (2), bleeding caused by the rupture of esophageal varices (2), and unknown causes (4). All patients had been in hepatic coma for 2-4 days before L-dopa therapy was instituted. All 10 patients recovered consciousness 6 hr to 4 days after therapy was begun; 8 recovered and 2 died (1 after 22 days of bleeding varices and 1 after 3 days of bronchopneumonia). After administration of L-dopa 1 patient became irritable and aggressive, developed insomnia, and had a temporary increase in blood pressure; after recovering consciousness palpitations and tachycardia developed, but an electrocardiogram showed no evidence of arrhythmia. One jaundiced patient had increases in direct and indirect bilirubin. No patients vomited, and all had increased appetites. All patients had increases in SGOT, SGPT, and LDH activities. Urinary serotonin values were variable. Blood ammonia concentrations, which were generally high, decreased after recovery of consciousness in some patients; in others they followed an irregular course. A positive Coombs reaction became negative in 1 case. Euglobulin and fibrinogen lysis, which were low in some patients, decreased even further during treatment and then normalized. During recovery of consciousness, electroencephalograms showed disappearance of δ-rhythm and structuring a α-rhythm to 8 cycles/sec with good reactivity. L-dopa was also administered to 2 patients who are not included in this series. These patients were very ill and died a few hours after administration of the drug.

6050 ESTROGEN-ANDROGEN IMBALANCE IN HEPATIC CIRRHOSIS. STUDIES IN 13 MALE PATIENTS.

(E.) Chopra, I. J.; Tulchinsky, D.; Greenway, F. L. (Univ. California Ctr. Hlth. Sci., Los Angeles). *Ann. Intern. Med.* 79(2):198-203, 1973.

Serum concentrations of testosterone, dihydrotestosterone, estradiol-17β (E_2), and gonadotrophins were studied in 13 male patients (aged 35-59 yr) with chronic hepatic cirrhosis. All had histories of alcohol abuse ranging from 3-30 yr duration. Ascites was present in 12 cases, esophageal varices in 6, spider angiomata in 9, testicular atrophy in 10, and gynecomastia in 6. The mean serum total testosterone concentrations were significantly lower in the cirrhotic patients (234 ng/100 ml) than in normal men (568 ng/100 ml). Unbound testosterone concentrations were lower in cirrhotic patients (5.79 ng/100 ml) as compared to normal men (15.6 ng/100 ml). Serum dihydrotestosterone levels were also subnormal in 5 of 6 patients studied. On the other hand, the mean serum total and unbound E_2 concentrations were significantly higher in patients with cirrhosis (total E_2=4.7 ng/100 ml) than in normal men (total E_2=2.7 ng/100 ml). The most consistent abnormality and the one uniformly present was a supranormal E_2 to testosterone ratio, as calculated from serum concentration of total or unbound steroids. These findings suggest that changes in the relative balance between circulating estrogen and androgen play some part in the pathogenesis of gynecomastia in hepatic cirrhosis. The mean serum luteinizing hormone concentration was elevated in patients with cirrhosis, whereas that of follicle-stimulating hormone did not differ from normal.

6051 STUDY OF IRON ABSORPTION IN CIRRHOTICS.

(Sp.) de Portugal-Alvarez, J.; Garcia Albarran, J.; Grino Prieto, E.; Gallardo Polo, L. E. (San Carlos Clin. Hosp., Univ. Madrid, Spain). *Rev. Clin. Esp.* 125(4):295-300, 1972.

Intestinal absorption of ^{59}Fe (15 µCi with nonradioactive carrier and vitamin C) was measured in 15 normal subjects and in 15 patients with cirrhosis. Fecal excretion of ^{59}Fe was measured for 7 days; none of the cirrhotics bled during the test. Iron absorption was significantly increased in cirrhosis (38.3 ± 14.2% versus 23 ± 7.9% in controls). Of the 15 cirrhotics, 7 had a history of chronic alcoholism, 5 nonalcoholics had a history and/or histological evidence of hepatic necrosis, and the etiology could not be identified from history or histology in 3 cases. No significant differences in ^{59}Fe absorption were observed between the 3 etiological types of cirrhosis. No correlations were observed between ^{59}Fe absorption and hematological parameters (hematocrit, hemoglobin, mean corpuscular hemoglobin concentration, reticulocyte count, Fe concentration, transferrin saturation coefficient, half-life of ^{59}Fe, or plasma Fe turnover). A study of iron kinetics, made on 7 cirrhotics, revealed that absorption of ^{59}Fe was significantly higher in patients with low levels of iron in the blood. Intestinal ^{59}Fe absorption was significantly higher in 3 patients with no evidence of Fe deposits in the liver than in 5 with large or moderate Fe deposits. ^{59}Fe absorption was also higher in 2 patients with total iron deficiency (blood and liver) than in 2 with no Fe deficiency.

6052 HEPATIC ENCEPHALOPATHY.

(E.) Losowsky, M. S.; Scott, B. B. (St. James's Hosp., Leeds, England). *Br. Med. J.* 3(5874):279-281, 1973.

The following mechanism of hepatic encephalopathy is advanced. Toxic products of bacterial degradation of nitrogenous material in the bowel are not removed by the liver when chronic liver disease exists and thus reach the brain. Ammonia may be one of the toxic products responsible for hepatic encephalopathy; it is certainly not the only one. Examinations of patients dying after long hepatic encephalopathy reveal swelling and increasing numbers of the protoplasmic astrocytes in various parts of the brain and, in severe cases, degeneration of nerve cells of the basal ganglia and cerebral cortex. These changes bear some relation to the duration and severity of the encephalopathy and are characteristic of advanced liver disease. It is suggested that these structural changes are related to the permanent neurological sequelae of prolonged encephalopathy rather than to the usual reversible signs. Factors which are thought to precipitate encephalopathy include gut bleeding, potassium depletion, acetazolamide, uremia, fluid and electrolyte abnormalities, sedatives, infection and constipation. Methods of treatment must be designed to reduce the amount of nitrogenous products in the bowel, their breakdown by bacteria, or their absorption. A positive response to measures aimed at these objectives offers confirmatory evidence that the particular symptoms are indeed due to hepatic encephalopathy.

6053 OXYGEN AFFINITY OF HEMOGLOBIN AND RED CELL 2,3-DIPHOSPHOGLYCERATE IN HEPATIC CIRRHOSIS.

(E.) Astrup, J.; Rorth, M. (Bispebjerg Hosp., Copenhagen, Denmark). *Scand. J. Clin. Lab. Invest.* 31(3): 311-317, 1973.

The level of 2,3-diphosphoglycerate in erythrocytes increased in 52 patients with cirrhosis of the liver, and, as a consequence, the oxygen affinity of hemoglobin was decreased. Part of the 2,3-diphosphoglycerate in the cirrhosis patients was caused by a concomitant anemia. At all hemoglobin levels, however, patients with cirrhosis showed an additional 2,3-diphosphoglycerate increase in comparison with patients without cirrhosis. Red cell 2,3-diphosphoglycerate was positively correlated to pH in plasma and in erythrolysate. It is likely that pH changes contributed to the regulation of the red cell 2,3-diphosphoglycerate concentration in cirrhotic patients. In 48 of these patients, the arterial pH and pCO_2 did not differ significantly from normal values. Other, as yet unknown, factors presumably contribute to the increase in red cell 2,3-diphosphoglycerate. No direct effect of NH^+ on red cell 2,3-diphosphoglycerate could be demonstrated *in vitro*. The plasma concentration of NH^+ *in vivo* correlated positively to plasma pH. The lowered oxygen affinity does not contribute significantly to the decrease in oxygen saturation of arterial blood often found in patients with hepatic cirrhosis.

6054 TREATMENT OF BLEEDING ESOPHAGEAL VARICES IN CIRRHOSIS AND ITS RESULTS. *(Ger.)* Schuster, G.; Ungeheuer, E. (Northwest Hosp., Frankfurt/Main-Praunheim, Germany). *Med. Klin.* 67(19):668-671, 1972.

Of 241 cirrhotics treated between 1964-1971 for bleeding esophageal varices, the highest mortality (65.1%) occurred among the 43 patients treated with palliative surgery; this was followed by a 26.0% mortality among the 50 treated by conservative methods alone. Best results (1 death out of 6) were obtained with shunt operations. These findings were confirmed on a group of 247 patients treated between 1964-1971 for bleeding esophageal varices. In contrast to 93 cirrhotics treated conservatively (mortality 72.04%) and 43 treated with palliative surgery (mortality 65.11%), only 13 of 111 patients who underwent shunt surgery died (mortality 11.7%). Since palliative surgery does not relieve portal hypertension, shunt operations should be performed if total bilirubin is 2 mg/100 ml or less, BSP retention is less than 30%, transaminase values are no more than 50-70 milliU/ml, total protein is over 6 g/100 ml, albumin is over 3 g/100 ml, and the patient does not have ascites. Hepatic coma does not occur more frequently after shunt operations than in patients treated conservatively or with palliative surgery.

6055 METABOLIC REFLECTION OF FRUCTOSE INFUSION IN CIRRHOTIC PATIENTS AND THE EFFECT OF TOLBUTAMIDE AND BUTYLBIGUANIDE. *(E.)* Brodanova, M.; Brodan, V.; Kordac, V.; Marecek, Z.; Slabochova, Z.; Kuhn, E. (Fac. Gen. Med., Charles Univ., Prague, Czechoslovakia). *Acta Hepato Gastroenterol.* 19(2): 116-124, 1972.

6056 DYNAMIC STUDY OF CARBOHYDRATE METABOLISM IN HEPATIC CIRRHOSIS. DETERMINATION OF FREE FATTY ACIDS AND INSULIN BLOOD LEVELS. *(Fr.)* Perreau, P.; Joubaud, F.; Cheguillaume, J.; Boyer, J.; Vernin, H. (Univ. Hosp. Ctr., Angers, France). *Sem. Hop. Paris* 48(14):957-966, 1972.

6057 AUSTRALIA ANTIGEN IN CIRRHOSIS. A STUDY OF 45 PATIENTS IN TURKEY. *(E.)* Demirel, N.; Pirnar, A.; Telatar, H.; Karacadag, S. (Hacettepe Univ. Med. Ctr., Ankara, Turkey). *Am. J. Gastroenterol.* 59(4):332-335, 1973.

6058 PORTAL DRAINAGE INTO THE LEFT RENAL VEIN IN PATIENTS WITH CIRRHOSIS. *(E.)* Mazzoni, G.; Di Martino, C. (Vittorio Emanule III Hosp., Valmontone, Italy). *Surg. Gynecol. Obstet.* 137(7): 487-488, 1973.

6059 PORTAL DECOMPRESSION: CLINICAL EXPERIENCE WITH THE "H" GRAFT. *(E.)* Graziano, J. L.; Sullivan H. J. (VA Hosp., Hines, Ill.). *Ann. Surg.* 178(2):209-214, 1973.

6060 TWO AUTOPSY CASES OF GLYCOGEN STORAGE DISEASE - CIRRHOTIC TYPE. *(E.)* Motoi, M.; Sonobe, H.; Ogawa, K.; Murakami, M.; Yamanouchi, I.; Toda, H.; Okamoto, T.; Ohara, T. (Okayama Univ. Med. Sch., Japan). *Acta Pathol. Jap.* 23(1):211-223, 1973.

6061 SIGNIFICANCE OF LAPAROSCOPIC DIAGNOSIS OF PORTAL HYPERTENSION FOR LIMITING PROTEIN INTAKE IN PATIENTS WITH CIRRHOSIS. *(Ger.)* Leonhardt, H.; Bungert, H. J. (Steglitz Clin., Free Univ. Berlin, Germany). *Med. Welt* 43(23): 1525-1527, 1972.

6062 LIVER REGENERATION AFTER BILIARY CIRRHOSIS. *(Fr.)* Schmidt, B. J.; Pinus, J.; Patricio, F. R. S.; Jorge, N. (Paulista Sch. Med., Sao Paulo, Brazil). *Helv. Paediatr. Acta* 27(3): 299-307, 1972.

6063 HEMODYNAMIC INTERRELATIONS IN PORTAL HYPERTENSION CAUSED BY CIRRHOSIS OF THE LIVER. *(Sp.)* Garcia Civera, R.; Benages Martinez, A.; Lopez Merino, V.; Garcia-Conde Gomez, F. J. (Fac. Med. Valencia, Spain). *Rev. Esp. Enferm. Apar. Dig.* 38(1):19-34, 1972.

See also, 5750, 5752, 5753, 5761, 5769, 5788, 5970, 5972, 6034, 6044, 6046, 6113.

Gallbladder and Biliary Tract Diseases

6064 ACTIVITY OF α-1,4-GLUCOSIDASE IN EXTRAHEPATIC CHOLESTASIS AND ACUTE VIRAL HEPATITIS.

(E.) Gamklou, R.; Iwarson, S. (Sahlgrenska Hosp., Goteborg, Sweden). *Scand. J. Clin. Lab. Invest.* 31(3):327-330, 1973.

Since a release of acid phosphatase and arylsulfatase from liver lysosomes has been reported for extrahepatic cholestasis, and an increased basal activity of β-glucuronidase and acid phosphatase has been found in liver specimens from patients with acute hepatitis, the present study was carried out to test for similar changes in the activity of lysosomal α-1,4-glucosidase in the 2 diseases. It was found that in patients with extrahepatic cholestasis (6 males and 16 females, aged 18 to 62 yr), the activity of α-1,4-glucuronidase in homogenates of liver biopsies was decreased, while the activity in the serum was unchanged, compared to healthy control subjects. This result suggests an impaired synthesis of the enzyme in patients with this disease. In patients with acute viral hepatitis (17 males and 12 females, aged 17 to 72 yr), the activity of α-1,4-glucosidase in the serum was the same as it was in normal subjects.

6065 POLYARTERITIS NODOSA OF THE GALLBLADDER, PRESENTING AS ACUTE CHOLECYSTITIS. *(E.)*

LiVolsi, V. A.; Perzin, K. H.; Porter, M. (Columbia Univ. Coll. Phys. Surgeons, New York, N.Y.). *Gastroenterology* 65(1):115-123, 1973.

Gallbladder involvement has been found at time of autopsy in 10 to 40% of patients with polyarteritis nodosa. Rarely, however, is acute cholecystitis the initial clinical manifestation of this disorder. In the present report, case reports for 4 patients (3 males and 1 female, aged 33-66 yr) are presented in whom the diagnosis of polyarteritis nodosa was first made by pathological examination of a gallbladder surgically removed for acute cholecystitis. It is concluded that if acute cholecystitis is found in the absence of cholelithiasis or other obvious cause, the gallbladder should be examined with multiple sections because the vascular changes of polyarteritis are usually focal and may be missed if only routine random sections are taken. Because steroid therapy improves the prognosis in this disease, clinicians and pathologists should be aware of this unusual occurrence.

6066 ASSESSMENT OF THE ^{14}C-GLYCOCHOLIC ACID BREATH TEST. *(E.)*

James, O. F. W.; Agnew, J. E.; Bouchier, I. A. D. (Roy. Free Hosp., London, England). *Br. Med. J.* 3(5873):191-195, 1973.

The 1-(^{14}C)-glycine-glycocholic acid breath test was performed on 104 subjects and a normal range established. In addition to 34 normal controls, subjects with the following diseases were included: ileal resection (6), cholangitis (6), primary biliary cirrhosis (12), other hepatobiliary disease (17), post Polya gastrectomy (4), ulcerative colitis (8), Crohn's disease (4), celiac disease (3), small bowel lymphoma (2), chronic pancreatitis (2), nodular lymphoid hyperplasia (1), gastrocolic fistula (2), jejunal diverticula (1), and staphylococcal enterocolitis (1). Abnormal results due to bacterial deconjugation of bile salts were found not only in patients with the "contaminated bowel" syndrome and in those with ileal resection, but also in patients with cholangitis. Abnormal results were also found in patients with gastrocolic fistula and staphylococcal enterocolitis, while mildly abnormal results were also found in some patients with liver disease. It is concluded that the ^{14}C-glycocholic acid breath test is a useful and simple screening test for detection of bacterial deconjugation of bile salts. It should be of value in the diagnosis of bacterial overgrowth syndromes and also in the evaluation of cholangitis.

6067 PRIMARY CARCINOMA OF THE GALLBLADDER.

(E.) Keill, R. H.; DeWeese, M. S. (Univ. Missouri Sch. Med., Columbia). *Am. J. Surg.* 125(6):726-729, 1973.

The clinical records of 33 patients (30 females and 3 males) treated at the University of Missouri Medical Center for carcinoma of the gallbladder were studied retrospectively. The patients ranged in age from 50-90 yr, with 85% over 60 yr. The most common symptom was abdominal pain (25 patients) followed by weight loss (20), nausea and vomiting (17), and jaundice (15). The duration of symptoms ranged from 1 week to 10 yr, averaging 12 1/2 months. Gallstones were present in 75.8%. The most common histologic type of tumor encountered was adenocarcinoma, but 12.1% of the tumors were adenoacanthoma. The mean survival time after operation was 2.95 months. There was no survivors beyond 13 months. On the basis of current information and knowledge, early cholecystectomy in all patients with calculous disease appears to offer the best hope for decreasing the distressingly high mortality associated with carcinoma of the gallbladder.

6068 THE NONOPERATIVE TREATMENT OF RETAINED STONES IN THE COMMON BILE DUCT. *(E.)*

Galloway, S. J.; Casarella, W. J.; Seaman, W. B. (Columbia-Presbyterian Med. Ctr., New York, N.Y.). *Surg. Gynecol. Obstet.* 137(1):55-58, 1973.

Retained gallstones were detected in 7 patients at T-tube cholangiography performed 8-12 days after biliary tract surgery. Before an attempt was made to remove stones nonsurgically the T-tube was allowed to remain in place for 3-6 weeks after choledochotomy to assure formation of a fibrous tract along the drainage tube. By using polyethylene or Coude-tipped catheters, small stones were flushed or mechanically pushed, or both, through the ampulla of Vater. Larger stones were removed from the common bile duct by passing a stone basket through a larger diameter tube or catheter inserted into the common bile duct *via* the fistulous tract of the T tube. Retained gallstones were successfully removed from 5 of the 7 patients treated. One failure was due to a small T-tube tract which prevented successful manipulation, and the other resulted from the size of the retained stone which had a diameter of 1.5 cm. No complications of the procedure have occurred and during follow-ups of 6 months to 2 yr no recurrent biliary colic or obstructive jaundice have appeared.

6069 TRANSIENT INCOMPETENCE OF THE SPHINCTER OF ODDI WITH PNEUMOBILIA: A CASE REPORT. *(E.)* Shariatzadeh, A. N.; Boliver, J. C. (Indiana Univ. Med. Ctr., Indianapolis). *Am. Surg.* 39(7):406-409, 1973.

A 45 yr old male presented with mild pain which began suddenly in the right upper quadrant of the abdomen. Shortly after admission, the pain spontaneously disappeared. An oral cholecystogram revealed air in the biliary tree. Gallstones were not found at this time, but were noted 2 weeks later. No abnormal communication was found between the biliary and gastrointestinal tracts either by roentgenography or at operation. The sudden onset, short duration, and spontaneous disappearance of pneumobilia was attributed in this case to migrating stones. It is suggested that the air in the biliary tract in this case, by exclusion, arose from a transient incompetence of the sphincter of Oddi following the passage of a small stone through the ampulla of Vater.

6070 DISSOLUTION KINETICS OF GALLSTONES: PHYSICAL MODEL APPROACH. *(E.)* Higuchi, W. I.; Sjuib, F.; Mufson, D.; Simonelli, A. P.; Hofmann, A. F. (Coll. Pharm., Univ. Michigan, Ann Arbor). *J. Pharm. Sci.* 62(6):942-945, 1973.

Recent studies suggested that *in situ* dissolution of gallstones in man might be dissolution-rate controlled. In this work, several physical models for the dissolution rate of cholesterol-type stones were developed. One is based on simple diffusion-controlled dissolution and another on a leaching process. Two others relate to interfacial coat-type barriers. Calculations were carried out employing models with reasonable input parameters. The results show, for example, that the theoretical dissolution rate based on the simple dissolution model would predict that a 2.5 mm stone should dissolve in several days into an undersaturated bile solution. Both clinical and *in vitro* experiments show that much longer times, e.g., months, are needed. The reason why observed rates are significantly slower than diffusion controlled may be clinically important.

6071 DISSOLUTION RATES OF CHOLESTEROL MONOHYDRATE CRYSTALS AND HUMAN CHOLESTEROL GALLSTONES IN BILE ACID-LECITHIN SOLUTIONS: ENHANCING EFFECT OF ADDED ALKYL QUATERNARY AMMONIUM SALTS. *(E.)* Higuchi, W. I.; Prakongpan, S.; Young, F. (Coll. Pharm. Univ. Michigan, Ann Arbor). *J. Pharm. Sci.* 62(7):1207-1208, 1973.

Benzalkonium chloride and other quaternary ammonium compounds were used to counteract or eliminate the interfacial barriers present in the cholate-lecithin media for cholesterol dissolution. Dissolution rates for 2% cholate, 2% cholate-0.5% benzalkonium, 2% cholate-1% lecithin, and 2% cholate-1% lecithin-0.5% benzalkonium chloride were 7.91, 1.31, 65.63, and 2.84 x 10^{-3} sec/cm, resp. For 5% cholate the values were similarly affected by added benzalkonium chloride. Similar effects were obtained using 0.5% cetylpyridinium chloride; 0.5% cetrimonium bromide was around 80% as effective as benzalkonium chloride. In experiments with cholesterolmonohydrate pellets, the dissolution rate was 61.76 x 10^3sec/cm without and 1.57 x 10^3sec/cm with benzalkonium chloride. These results and the methodology reported with benzalkonium chloride and other quaternary ammonium compounds may prove useful in finding or designing safe and efficacious agents or therapeutic regimens for the medical treatment of gallstones.

6072 ROUTINE OPERATIVE CHOLANGIOGRAPHY. ANALYSIS OF 506 CONSECUTIVE CHOLECYSTECTOMIES. *(E.)* Saltzstein, E. C.; Evani, S. V.; Mann, R. W. (Mt. Sinai Med. Ctr., Milwaukee, Wis.). *Arch. Surg.* 107(2):289-291, 1973.

Transcystic duct operative cholangiography was performed in 423 of 506 consecutive cholecystectomies. Patients (25% males and 75% females; aged 14-86 yr with the majority between 40-60 yr of age) were classified prospectively as having or not having a preoperative clinical indication for common duct exploration on the basis of jaundice, pancreatitis, or an elevated alkaline phosphatase level. Of 79 patients, with positive preoperative clinical indications for common duct exploration, 39 (50%) had normal cholangiograms, and were spared exploration of the common duct by operative cholangiography. Of 427 patients without clinical indications for duct exploration, unsuspected common duct stones were demonstrated in 8 (1.8%). Routine operative cholangiography reduced the number of common duct explorations to 11.1% of cholecystectomies, and reduced negative common duct explorations to 3.2%. Therefore, it is suggested that the indication for operative cholangiography is "cholecystectomy."

6073 PRIMARY HYPERPARATHYROIDISM, PANCREATITIS, AND CHOLELITHIASIS. *(Ger.)* Brunner, H.; Rothmund, M. (Surg. Clin., Univ. Mainz, Germany). *Dtsch. Med. Wochenschr.* 98(9):426-429, 1973.

Of 23 patients with primary hyperparathyroidism, 8 had cholelithiasis, cholecystitis, or choledocholithiasis; 4 patients (2 men and 2 women, aged 37-48 yr) of these 8 developed recurrent pancreatitis. In all cases the patients' symptoms disappeared after removal of parathyroid adenomas and hyperplastic parathyroid tissue. Parathyroid adenomas were removed from 3 patients and the other underwent surgery for 2 eutropic adenomas in the neck and struma aberrata with dystopic parathyroid tissue in the thorax. The latter patient, who had the most severe and protracted course, had cholecystitis and severe choledocholithiasis with incrusted gravel in the retroduodenal bile duct and papillary region. In this case it is possible that the pancreatitis was biliary in origin. Although some authors believe that both pancreatitis and gallstones are secondary to primary hyperparathyroidism, it is more likely that the pancreatitis is biliary in origin. Only calcareous pancreatitis or pancreatolithiasis associated with gallstones should be regarded as a consequence of disturbances in calcium metabolism.

6074 PRIMARY CARCINOMA OF THE EXTRAHEPATIC BILE DUCTS.

(E.) Yarbrough, III., D. R. (Med. Univ. South Carolina, Charleston). *Am. J. Surg.* 125(6):723-725, 1973.

A series of 15 patients (11 females and 4 males, aged 45-77 yr) with a diagnosis of carcinoma of the extrahepatic bile ducts was studied. Chief complaints at the time of diagnosis were jaundice (14), pain (10), weight loss (10), palpable mass (6), and pruritis (11). Of the 15 patients, 2 had a history of preexisting disease of the biliary tract, 1 having undergone cholescystectomy for chronic cholecystitis and cholelithiasis 7 months prior to this diagnosis. A second patient underwent cholecystectomy for acute cholecystitis with cholelithiasis 4 yr earlier. At diagnosis total bilirubin ranged from 1-30 mg% and alkaline phosphatase from 6.6 to 51 King-Armstrong U. In the 9 patients available for follow-up, survival ranged from 5 days to 15 months after surgery. Of the 3 patients who had drainage of the common bile duct, follow-up studies were performed on 2 and the average surval time was 12 months. Patients undergoing exploratory laparotomy and biopsy only survived an average of less than 1 month. The longest survival occurred in the 1 patient who received a therapeutic regimen of 5-fluorouracil after exploratory laparotomy, biopsy, and decompression of the bile duct via a T-Y tube.

6075 TAUROCHOLATE METABOLISM IN PATIENTS WITH CHOLESTEROL GALLSTONES.

(E.) Arnesjo, B.; Stahl, E. (Univ. Hosp., Lund, Sweden). *Scand. J. Gastroenterol.* 31(3):369-375, 1973.

Tracer doses of doubly labelled taurocholate, ^{35}S-tauro-7-^{3}H-cholate, were given p.o. to 10 patients with cholesterol gallstones but functioning gallbladders, and duodenal aspirates were examined for the next 7 days. Taurocholate pool size was 0.3 g, which was significantly smaller than that of the healthy group. Half-life of the taurocholate pool was 1.1 days, which was significantly lower than in the controls. Daily production of taurocholate was no different. 7-α-Dehydroxylation was about twice as high. Fractional deconjugation rate was 0.59/day, which was an increase of low significance. A significantly lower trihydroxy to dihydroxy bile acid ratio was found. It is suggested that this relative increase of dihydroxycholanic acids in the bile might favor gallstone formation.

6076 AN EPIDEMIOLOGIC APPROACH TO CHOLECYSTOGRAPHY. A PILOT STUDY IN ONTARIO.

(E.) Bobechko, P. E.; Davidson, J. W. (Dept. Radiol., Univ. Toronto, Canada). *J. Can. Assoc. Radiol.* 24:18-23, 1973.

Information collected from 1767 Ontario patients at time of cholecystography was analyzed to determine factors possibly related to gallbladder disease. The results were comparable with well-known etiologic factors such as age and sex. A significantly higher percentage of gallbladder disease was present in females, with the frequency of gallstones in both males and females increasing with advancing age. Among female patients, increased weight was accompanied by increased incidence of disease. The percentage of abnormal examinations increased as the number of pregnancies increased, particularly after the 4th pregnancy. An increased frequency of gallbladder disease was demonstrated in recent female immigrants from the U. K. No influence in the ratio of abnormal examinations to normals in those female patients with positive family histories was demonstrated. However, the higher frequency of abnormal cholecystograms in male patients with a positive family history suggested that a sex-linked factor, not previously described, may be implicated.

6077 ORAL CONTRACEPTIVES AND VENOUS THROMBOEMBOLIC DISEASE, SURGICALLY CONFIRMED GALLBLADDER DISEASE, AND BREAST TUMOURS.

(E.) Greenblatt, D. J.; Ory, H. W.; Levy, M. (Boston Collaborative Drug Surveillance Program, Mass.). *Lancet* (7817):1399-1404, 1973.

Associations between oral contraceptive use and venous thromboembolism and gallbladder disease in women aged 20-44 yr were established by a survey covering 24 hospitals in the Boston area. Of 43 patients with idiopathic venous thromboembolism, 31 (72%) used oral contraceptives. Of 212 patients with gallbladder disease, 65 (31%) were oral contraceptive users. In the 842 healthy controls used in both studies, the frequency of oral contraceptive use was 20%. Compared with nonusers, the relative risk for thromboembolism in oral contraceptive users is 11, and the attack rate attributable to the contraceptives is 60/100,000 users/yr. It is not clear whether the clinical association between oral contraceptives and thromboembolic disease is accounted for by changes in the coagulation mechanism. The corresponding relative risk for gallbladder disease is 2.0, and the estimated annual attack rate is 79/100,000 users. In women below age 35, the frequency of gallbladder disease was significantly higher in those taking oral contraceptives for 6-12 months compared with women who took them for longer periods. It is suggested that hormonal differences between the sexes may account for the greater incidence of gallbladder disease in women of childbearing age compared with men, and that oral contraceptives may potentiate the risk. Experimental evidence indicates that estrogen alters bile composition. As nearly all women in the survey took low-dose estrogen preparations, the role of dosage could not be evaluated. No evidence of a positive association between oral contraceptives and breast tumors was demonstrated.

6078 FACTORS INFLUENCING THE TIMING OF CHOLECYSTECTOMY IN ACUTE CHOLECYSTITIS. *(E.)* Gardner, B.; Masur, R.; Fumimoto, J. (State Univ. New York Downstate Med. Ctr., Brooklyn). *Am. J. Surg.* 125(6):730-733, 1973.

A review of 256 patients (46 males and 210 females) with acute cholecystitis revealed that morbidity was lower with early operation. Delayed operation was associated with a higher morbidity and no difference in mortality in patients under 69 yr of age. In patients over 69, acute cholecystitis necessitating cholecystectomy carried a prohibitive mortality. Therefore, more use should be made of planned cholecystostomy with the patient under local anesthesia. Jaundice, present in 88 cases, did not play a significant role in mortality of patients operated on immediately but may have been associated with increased mortality in those patients in whom operation was delayed. Pancreatitis occurred in 44 cases preoperatively and, although it did not constitute a contraindication to early operation, its presence was associated with higher complication rates regardless of when surgery was performed. Leukocytosis and an abdominal mass were factors leading to a more aggressive operative approach. Preoperative antibiotics did not decrease the postoperative complication rate in cholecystectomy for acute cholecystitis and may effectively mask the signs necessary to indicate early operation. Early operation for acute cholecystitis is recommended because it effectively reduces morbidity and the length of hospital stay.

6079 CHOLEDOCHAL CYSTS: DIAGNOSTIC AND THERAPEUTIC PROBLEMS. *(E.)* Klotz, D.; Cohn, B. D.; Kottmeier, P. K. (State Univ. New York Downstate Med. Ctr., Brooklyn). *J. Pediatr. Surg.* 8(2):271-283, 1973.

Records of 8 patients with congenital biliary cysts were studied. The series included 5 newborns (4 males and 1 female) and 3 female patients aged 4, 7, and 37 yr. The correct diagnosis was anticipated in only 2, and several patients underwent prolonged nonoperative treatment because of a mistaken diagnosis of hepatitis. Even in patients with an abdominal mass the true character of the cyst was not suspected until a detailed radiographic work-up was completed. Of these 8 cases, 2 had association of proximal atresia and a 3rd had partial proximal obstruction. Also, 2 patients showed the association of extra- and intrahepatic congenital biliary cysts. The associated symptoms of pain, jaundice, and abdominal mass were completely lacking in this series. A study of these cases and 138 cases reported during the last 4 yr indicates that choledochal cysts represent only one of various biliary cystic dilatations that can occur in either an isolated or a multiple form. A review of operative procedures performed during the last decade reveals that excision and duct-enterostomy carry a mortality risk no higher than cyst-enterostomies, with fewer postoperative complications in a still-limited follow-up period.

6080 LIVER-CELL CARCINOMA PRESENTING AS BILE-DUCT TUMOR. *(E.)* Waldron, R. L.; Kenny, G.; Sorger, K. (Mount Auburn Hosp., Cambridge, Mass.). *Br. J. Radiol.* 46(3):195-197, 1973.

6081 MASSIVE GASTRO-INTESTINAL HAEMORRHAGE DUE TO BILIARY TRACT (HEMOBILIA). (REPORT ON 3 RARE CASES). *(E.)* Kourias, B.; Tsoufis, E. (Hosp. Athens, Greece). *Chir. Gastroenterol.* 6(4):388-394, 1972.

6082 GALLSTONES. PATHOGENESIS OF THE DIFFERENT FORMS. PATHOLOGICAL AND THERAPEUTICAL SIMILARITIES BETWEEN CHRONIC CHOLECYSTITIS AND ATHEROSCLEROSIS. *(E.)* Besancon, F. (Broussais Hosp., Paris, France). *Rendic. Gastroenterol.* 4(3):145-158, 1972.

6083 PATHOLOGICAL STUDIES ON CARCINOMA OF THE GALLBLADDER; ESPECIALLY ON THE RELATIONSHIP BETWEEN DEEP CHOLECYSTIC FOSSA AND OCCURRENCE OF CARCINOMA. *(E.)* Kojima, K.; Saito, K. (Ctr. Pathol., Welfare Fdn., Nagaoka, Japan). *Acta Med. Biol.* 19(2):151-163, 1971.

6084 HETEROTOPIC GASTRIC MUCOSA IN THE GALLBLADDER PRESENTING AS A SYMPTOM-PRODUCING TUMOR. A CASE REPORT. *(E.)* Bentivegna, S.; Hirschl, S. (New York Med. Coll., N.Y.). *Am. J. Gastroenterol.* 57(5):423-428, 1972.

See also, 5654, 5656, 5718, 5760, 5800, 5871, 5894, 5966.

6085 PROTECTION AGAINST ENTERIC BACTERIAL INFECTION BY SECRETORY IgA ANTIBODIES. *(E.)* Fubara, E. S.; Freter, R. (Univ. Michigan Med. Sch., Ann Arbor). *J. Immunol.* 111(2):395-403, 1973.

Purified antibody preparations obtained from the lumen of the intestine of orally vaccinated germfree mice, containing very small amounts of secretory IgA but no other serologically active immunoglobulins, protected mice against experimental enteric cholera infection. This protection was associated with a reduction in that fraction of the total *Vibrio* population which was adsorbed to the mucosa. Total counts of intestinal *Vibrio* populations were not affected. By using metabolic inhibitors in experimental infections of intestinal loops of rabbits the mechanism of this process was investigated. Iodoacetate reversed the antibody-mediated shift of the *Vibrio* population away from association with the mucosa. This suggests that the mucosal cell may furnish some accessory factor which, in conjunction with antibody, results in an antibacterial mechanism on the mucosal surface. Iodoacetate had no effect on total *Vibrio* population and adsorption of *Vibrio* in nonimmunized intestinal loops. Consequently, it is less likely that iodoacetate acts directly on *Vibrio*, rather than on the mucosal cells. These results suggest that intestinal secretory IgA in the intestine was active in protection against experimental cholera and this protection was associated with, if not directly caused by, the inhibition of *Vibrio* adsorption to the intestinal mucosa.

6086 INVASIVE ENTEROPATHIC ESCHERICHIA COLI DYSENTERY. AN OUTBREAK IN 28 ADULTS. *(E.)* Tulloch, Jr., E. F.; Ryan, K. J.; Formal, S.; Franklin, F. A. (Walter Reed Army Med. Ctr., Washington, D.C.). *Ann. Intern. Med.* 79(1):13-17, 1973.

Of 37 persons who ate mushrooms stuffed with contaminated, imported French Camembert cheese, 28 (over 75% aged 20-55 yr.) became ill with acute gastroenteritis within 24-48 hr. An 0124 *Escherichia coli* was isolated from the cheese and from the stools of 9 ill individuals. Biological testing showed this organism to be invasive in character. The predominant symptoms were fever, malaise, tenesmus, abdominal cramping, diarrhea, nausea and vomiting. None of the patients required hospitalization or antibiotic therapy, and most were asymptomatic within 1 week. This epidemic was part of the first known outbreak of invasive *E. coli* dysentery in adults occurring in the United States.

6087 GASTRO-INTESTINAL CELL LOSS IN MAN. ITS MEASUREMENT AND SIGNIFICANCE. *(E.)* Croft, D. N.; Cotton, P. B. (St. Thomas' Hosp., London, England). *Digestion* 8(2):144-160, 1973.

The rate of DNA loss from the epithelial surface of human stomach, small intestine, large intestine, and skin measures the rate of cell loss. From the data it is apparent that 287 g cells are lost every 24 hr from the mucosa of the entire human gastrointestinal tract. Evidence suggests that in the steady-state this loss reflects the rate of production or turnover of surface epithelial cells. In atrophic gastritis, celiac syndrome, exfoliative psoriasis, and possibly ulcerative colitis, the turnover is high. The rate of cell loss in these diseases is high/unit of surface area. In patients with celiac syndrome who are losing weight (active celiacs), small bowel DNA rates are particularly high, and they fall to normal after successful treatment. Results indicate that in malabsorptive states, iron, protein, fat, and folic acid are lost from the gut in excessive quantities. This increased endogenous loss of iron, protein, and fat is related to the increased loss of DNA or cells. In the case of protein, about 80 g are lost from the normal human small intestine/day, only 8-15% of which is derived from protein within cells. In the case of lipids, 12-30 g are lost/day from the human small bowel mucosa and it is virtually all derived from intracellular lipid within exfoliated epithelial cells. The term exfoliative enteropathy is suggested for this mechanism. It is indicated that excessive loss of endogenous material due to exfoliative enteropathy is an important cause of the malnutrition that results from diffuse diseases of the small intestine.

6088 NEUROLOGIC COMPLICATIONS OF GASTROINTESTINAL TRACT DISEASES. *(E.)* Rodgers, J. B. (Union Univ., Albany, N.Y.). *N.Y. State J. Med.* 73(8):971-976, 1972.

6089 LONG TERM REMISSION OF INOPERABLE GASTROINTESTINAL LYMPHOSARCOMA AFTER MASSIVE CHEMOTHERAPY. *(E.)* Hazeghi, P.; Lopez, J.; Cox, J. N.; Wyss, M. (Univ. Geneva, Switzerland). *Helv. Paediatr. Acta* 28(1):27-35, 1973.

6090 REDUCED PERITONEAL CLEARANCES IN SCLERODERMA INCREASED BY INTRAPERITONEAL ISOPROTERENOL. *(E.)* Brown, S. T.; Ahearn, D. J.; Nolph, K. D. (Univ. Missouri, Columbia). *Ann. Intern. Med.* 78(6):891-894, 1973.

6091 MASS INFECTIONS WITH SHIGELLA FLEXNERI 3A IN THE CITY HOSPITAL IN LODZ. I. EPIDEMIOLOGIC ANALYSIS. *(E.)* Libich, M.; Gzik, W.; Niedzielska, H.; Chizynski, Z. (Clin. Inf. Dis., Lodz, Poland). *Epidemiol. Rev.* 26(1): 61-66, 1972.

6092 SOME DISEASES CHARACTERISTIC OF MODERN WESTERN CIVILIZATION. *(E.)* Burkitt, D. P. (Med. Res. Council, London, England). *Clin. Radiol.* 24(3):271-280, 1973.

6093 INCIDENCE OF AMYLOIDOSIS IN RHEUMATOID ARTHRITIS. SOME CLINICAL OBSERVATIONS.

(E.) Lender, M.; Wolf, E. (Shaare Zedek Hosp., Jerusalem, Israel). *Scand. J. Rheumatol.* 3(1):109-112, 1972.

6094 TRANEXAMIC ACID IN UPPER GASTROINTESTINAL HAEMORRHAGE. *(E.)* Cormack, F.; Chakrabarti, R. R.; Jouhar, A. J.; Fearnley, G. R. (Gloucestershire Roy. Hosp., England). *Lancet* 1(7814):1207-1208, 1973.

6095 THE TOXIGENIC DIARRHEAS. *(E.)* Gorbach, S. L. (VA Hosp., Sepulveda, Calif.). *Hosp. Practice* 8(5):103-110, 1973.

6096 CHRONIC DIARRHEA IN INFANTS AND CHILDREN: PART I. *(E.)* Poley, J. R. (Children's Mem. Hosp., Oklahoma Univ., Oklahoma City). *South. Med. J.* 66(9):1035-1049, 1973.

6097 EOSINOPHILIC GRANULOMA OF THE GASTROINTESTINAL TRACT. *(Ger.)* Adler, G. G. (Friedrichshain Munic. Hosp., Berlin, Germany). *Bruns Beitr. Klin. Chir.* 219(5):429-439, 1972.

6098 SOME CLINICAL AND LABORATORY FINDINGS IN PATIENTS INJECTED WITH THORIUM DIOXIDE. STUDY OF 155 CASES. *(E.)* Saragoca, A.; Tavares, M. H.; Barros, F. B.; Horta, J. D. S. (Sch. Med., Univ. Lisbon, Portugal). *Am. J. Gastroenterol.* 57(4):301-310, 1972.

6099 ON PRIMARY GASTROINTESTINAL LYMPHOMA IN IRAQ. EXPERIENCE WITH 47 PATIENTS. *(E.)* Al-Bahrani, Z. R. (Med. City Hosp., Baghdad Univ., Iraq). *J. Med. Liban.* 25(6):453-475, 1972.

6100 PRIMARY SEBACEOUS CARCINOMA OF THE PAROTID GLAND. *(E.)* Akhtar, M.; Gosalbez, T. G.; Brody, H. (Albert Eistein Med. Ctr., Philadelphia, Pa.). *Arch. Pathol.* 96(3):161-163, 1973.

6101 ARTERIOVENOUS FISTULA OF THE MESENTERY. *(E.)* Anderson, R. D.; Liebeskind, A.; Lowman, R. M. (Yale-New Haven Hosp., Conn.). *Am. J. Gastroenterol.* 57(5):453-458, 1972.

6102 ZOLLINGER-ELLISON SYNDROME. *(E.)* Isenberg, J. I.; Walsh, J. H.; Grossman, M. I. (VA Wadsworth Hosp. Ctr., Los Angeles, Calif.). *Gastroenterology* 65(1):140-165, 1973.

6103 WOLMAN'S DISEASE: REPORT OF TWO NEW CASES, WITH A REVIEW OF THE LITERATURE. *(E.)* Raafat, F.; Hashemian, M. P.; Abrishami, M. A. (Ahari Hosp., Tehran, Iran). *Am. J. Clin. Pathol.* 59(4):490-497, 1973.

6104 AUTOGENOUS FAT INSTILLATION FOR THE PREVENTION OF RECURRING ADHESIONS. *(E.)* Hauschild, W. A. (no affil.). *Abdom. Surg.* 15(3):62-64, 1973.

6105 THE LAXATIVE EFFECT OF PURE SENNOSIDES A AND B. *(E.)* Gothoni, G.; Nyberg, W.; Jokipii, S. G. (Res. Lab. Medica Ltd., Helsinki, Finland). *Ann. Clin. Res.* 5(1):46-48, 1973.

See also, 5721, 5751, 5768, 5778, 5783, 5789, 5796, 5878, 5949.

GENERAL

Parasitology

6106 THE PRESENCE OF HOST IMMUNOGLOBULINS IN HYDATID CYST MEMBRANES. *(E.)* Varela-Diaz, V. M.; Coltorti, E. A. (Pan American Health Org., W.H.O., Buenos Aires, Argentina). *J. Parasitol.* 59(3):484-488, 1973.

Mouse and sheep IgG immunoglobulins were detected by the immunoelectrophoresis test in the membranes of hydatid cysts obtained from these 2 host species. Both donor and recipient immunoglobulins were detected in the parasite membranes 3 months after transplantation of mouse hydatid cysts into guinea pigs. Since it seems likely that these immunoglobulins originated from the host and were not synthesized by he parasite, the ideas of natural selection, host nduction, phenotypic adaptation, or bound host ntibody may be disregarded. The presence of host gG in the hydatid cyst membrane indicates that in hemical analysis of structural proteins and amino cids of metacestodes and other helminths, the dif- erentiation of parasite components from host immuno- lobulins may be difficult to assess. These findings lso suggest that false positive reactions may arise hen antigens prepared from cyst membranes are used n hydatid serology. It is felt that the immuno- lectrophoresis test using a defined antigen is of alue in characterizing antigens in parasite membranes.

107 SPORADIC ANICTERIC LEPTOSPIROSIS IN SOUTH VIETNAM. A STUDY IN 150 PATIENTS. *(E.)* erman, S. J.; Tsai, C.; Holmes, K.; Fresh, J. W.; atten, R. H. (U.S. Naval Med. Res. Unit No. 2, aipei, Taiwan). *Ann. Intern. Med.* 79(2):167-173, 973.

n 150 American servicemen in Vietnam, leptospiral nfections caused the abrupt onset of fever, chills, nd headache. Myalgias and gastrointestinal com- laints were common. The most characteristic physi- al findings were muscle tenderness (42%) and con- unctivitis (42%). Aseptic meningitis was a compli- ation in 9 patents. Oliguria and azotemia of renal rigin occurred in 7, but none required dialysis. nly 2 patients became jaundiced; however, some liver unction tests were abnormal in 40% of the patients. here were no deaths. The clinical diagnosis depen- ed on recognizing the syndrome of muscle tenderness, onjunctivitis, and gastroenteritis in a febrile atient from an endemic area. In 1/3 of the patients, here were no abnormal findings other than fever, and he leptospiral infection would not have been detec- ed without serological surveillance of febrile atients from endemic areas. Treatment with tetra- ycline (2-4 g/day for an average of 4.9 days) did ot appear to alter the course of illness.

108 CLINICAL AMOEBIASIS SYNDROME AND CASE REPORTS OF A FEW UNUSUAL CASES OF AMOEBIA- IS. *(E.)* Kasliwal, R. M. (S.M.S. Med. Coll., aipur, India). *Am. J. Proctol.* 24(4):326-336, 973.

6109 TREATMENT OF AMOEBIASIS. *(E.)* Bell, D. R. (Liverpool Sch. Tropical Med., England). *Trop. Doct.* 3(3):140-143, 1973.

6110 RESISTANCE OF PIGS RECOVERED FROM TRANSMISSIBLE GASTROENTERITIS AGAINST INFECTION WITH ASCARIS SUUM. *(E.)* Gaafar, S. M.; Dugas, S.; Symensma, R. (Sch. Vet. Sci., Med., Purdue Univ., Lafayette, Ind.). *Am. J. Vet. Res.* 34(6):793-795, 1973.

6111 PROGRESS REPORT: INTESTINAL PARASITES. *(E.)* Knight, R.; Schultz, M. G.; Hoskins, D. W.; Marsden, P. D. (London Sch. Hyg. Trop. Med., England). *Gut* 14(2):145-168, 1973.

6112 PITFALLS IN THE DIAGNOSIS OF AMEBIC COLITIS. *(E.)* Wolloch, Y.; Chaimoff, C.; Zer, M.; Dintsman, M. (Beilinson Hosp., Petah Tiqva, Israel). *Dis. Colon Rectum* 16(1):42-45, 1973.

6113 ENZYME-HISTOCHEMICAL STUDIES ON RABBIT LIVER EXPERIMENTALLY INFECTED WITH FASCIOLA HEPATICA. *(E.)* Polyakova-Krusteva, O.; Krustev, L. (Central Helminthol. Lab., Acad. Sci., Sofia, Bulgaria). *Virchows Arch. (Zellpathol.)* 11(4):334-342, 1972.

See also, 5776, 5799.

GENERAL

Regional Enteritis

114 EXPERIENCE WITH ELEMENTAL DIET IN THE TREAT- MENT OF INFLAMMATORY BOWEL DISEASE. IS HIS PRIMARY THERAPY? *(E.)* Voitk, A. J.; Echave, V.; eller, J. H.; Brown, R. A.; Gurd, F. N. (McGill Univ. urg. Clin., Montreal Gen. Hosp., Canada). *Arch. Surg.* 07(2):329-333, 1973.

nflammatory bowel disease was treated with elemental iet 17 times in 13 patients for an average of 22 days. Regional enteritis was present in 7 patients, ulcerative colitis in 4, and radiation enteritis in 3. In 1 case regional enteritis and ulcerative colitis coexisted. In 4 patients some degree of short bowel syndrome was evident and 3 suffered from intestinal fistulas. The diet was well tolerated in all but 1 patient. All but one demonstrated weight gain and positive nitrogen balance, without apparent irritation of the inflamed gut. Surgery was indicated in

9 cases and 7 underwent operation, approaching it in an improved nutritional state and withstanding it well. Elemental diet is able to provide nutrition while allowing bowel rest, without the risks of i.v. hyperalimentation. Occasionally indications for surgery resolve during the period of nutritional improvement. Whether this represents a primary therapeutic effect of elemental diet or the natural course of the disease remains to be determined by controlled studies.

6115 REGIONAL ENTERITIS AND GROWTH RETARDATION WITHOUT INTESTINAL SYMPTOMS. *(E.)* Donald, J. W.; Donald, J. G. (no affil.). *South. Med. J.* 66(8):909-912, 1973.

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6117 ERYTHEMA MULTIFORME AND CROHN'S DISEASE OF THE LARGE INTESTINE. *(E.)* Brenner, S. M.; Delany, H. M. (Montefiore Hosp., Bronx, N.Y.). *Gastroenterology* 62(3):479-482, 1972.

6118 MERCURY AND THE GUT. *(E.)* Aaronson, R. M.; Spiro, H. M. (Yale Univ. Sch. Med., New Haven, Conn.). *Am. J. Dig. Dis.* 18(7):583-594, 1973.

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6121 LUPUS ERYTHEMATOSUS ASSOCIATED WITH CROHN'S DISEASE AFTER ANTI-TUBERCULOUS TREATMENT. *(Fr.)* Mornet, P.; Lafon, J.; Valleteau de Mouilliac, M.; Morin, M. (no affil.). *Sem. Hop. Paris* 49(30):2199-2207, 1973.

6122 30 CASES OF CROHN'S DISEASE. *(Fr.)* Mornet, P.; Guivarch, M.; Marquand, J.; Graveleau, J.; Mouchet, A.; Morin, M. (no affil.). *Sem. Hop. Paris* 49(30):2189-2198, 1973.

6123 AN EPIDEMIOLOGICAL STUDY OF REGIONAL ENTERITIS AND ACUTE ILEITIS IN COPENHAGEN COUNTY. *(E.)* Hoj, L.; Jensen, P. B.; Bonnevie, O.; Riis, P. (Gentofte Univ. Hosp., Hellerup, Denmark). *Scand. J. Gastroenterol.* 31(3):381-384, 1973.

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6125 AN EPIDEMIOLOGICAL STUDY OF REGIONAL ENTERITIS IN THE GLOUCESTER AREA. *(E.)* Tresadern, J. C.; Gear, M. W. L.; Nicol, A. (Gloucestershire Roy. Hosp., England). *Br. J. Surg.* 60 (5):366-368, 1973.

6126 THE MUSCULO-SKELETAL COMPLICATIONS OF GROHN'S DISEASE. *(E.)* Haslock, I.; Wright, V. (Gen. Infirm., Leeds, England). *Medicine* 52(3):217-225, 1973.

6127 CHOLESTYRAMINE: FACTORS LIMITING ITS ANTIDIARRHEAL EFFECT IN PATIENTS RESECTED FOR REGIONAL ENTERITIS. *(E.)* Sklar, M.; Uhri, V. (Wayne State Univ. Sch. Med., Detroit, Mich.). *Am. J. Gastroenterol.* 59(5):397-400, 1973.

6128 CROHN'S DISEASE OF THE APPENDIX. *(E.)* Howard, E. W.; Tuttle, J. R.; Jenis, E. H. (Walter Reed Army Med. Ctr., Washington, D. C.). *Am. Surg.* 39(6):349-354, 1973.

See also, 5931, 5934.

NUMBERS FOLLOWED BY AN ASTERISK INDICATE ABSTRACTS. OTHER NUMBERS REFER TO CITATIONS.

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NUMBERS FOLLOWED BY AN ASTERISK INDICATE ABSTRACTS. OTHER NUMBERS REFER TO CITATIONS.

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GASTROENTEROLOGY

ABSTRACTS
AND
CITATIONS

NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES

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PREFACE

GASTROENTEROLOGY ABSTRACTS and CITATIONS is a publication of the National Institute of Arthritis, Metabolism an Digestive Diseases. This specialized information medium has been initiated to fill an existing great need in the field of gastroenterology and to assist the Institute in meeting its obligations to foster and support laboratory and clinical research into the nature, causes, and therapy of diseases of the gastrointestinal tract Publication GASTROENTEROLOGY ABSTRACTS and CITATIONS makes available citations of all current papers relevant to this field from medical journals published throughout the world. Approximately one-third of the citations dealing with the major aspects of gastroenterology have accompanying abstracts.

The issuing of GASTROENTEROLOGY ABSTRACTS and CITATIONS under the auspices of the National Institute of Arthritis, Metabolism, and Digestive Diseases will provide a much needed current awareness tool to scientists and will facilitate greater integration of research and clinical efforts in this field. The number and great diversity of publications in the area of gastroenterology makes it imperative that an appropriate service be available to investigators and practitioners so that they may be apprised of progress with a minimum of delay. Our aim is to provide the readers with a readily systematized complilation of current published work. The publication will provide the greatest usefulness if these interested investigators will contribute their ideas and comments for consideration whenever possible.

GASTROENTEROLOGY ABSTRACTS and CITATIONS is published monthly and includes citations and abstracts from the biomedical world literature as they are currently received. Volume 7 will appear in, and be dated, 1973. There will be no hiatus in literature coverage from Volume 6 which was dated 1971. In addition, yearly cumulated subject and author indexes are published.

This publication is available free to National Institutes of Health grantees and contractors working in the field of gastroenterology and libraries of medical schools. Requests from these qualified individuals to receive free copies of this publication must include their grant or contract number and the title of their project. These requests as well as address changes and other communications should be addressed to:

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The Secretary of the Department of Health, Education, and Welfare has determined that the publication of this periodical is necessary in the transaction of the public business required by law of this Department. Use of funds for printing this periodical has been approved by the Director of the Office of Management and Budget through April 30, 1975.

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NOTE

Journal names are abbreviated according to the list of abbreviations used by *Index Medicus*. For journals not covered by *Index Medicus*, the abbreviations (with some modifications) found in *World Medical Periodicals*, 3rd Edition, are used.

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	It.	Italian
Ar.	Arabic	Jap.	Japanese
Bul.	Bulgarian	Kor.	Korean
Ch.	Chinese	Latv.	Latvian
Cz.	Czech	Lith.	Lithuanian
Dan.	Danish	Nor.	Norwegian
Dut.	Dutch	Pol.	Polish
E.	English	Por.	Portuguese
Eston.	Estonian	Rum.	Rumanian
Fin.	Finnish	Rus.	Russian
Fl.	Flemish	Ser.	Serbo-Croatian
Fr.	French	Sl.	Slovak
Ger.	German	Sp.	Spanish
Gr.	Greek	Sw.	Swedish
Heb.	Hebrew	Th.	Thai
Hun.	Hungarian	Turk.	Turkish
Ic.	Icelandic	Uk.	Ukrainian
In.	Indonesian	Viet.	Vietnamese

ABBREVIATIONS USED IN ABSTRACTS

ACTH	adrenocorticotropic hormone
ADP	adenosine diphosphate
AMP	adenosine monophosphate
ATP	adenosine triphosphate
BSP	sulfobromophthalein
C	degrees centigrade
cm	centimeter(s)
CNS	central nervous system
cpm	counts per minute
DNA	deoxyribonucleic acid
e.g.	for example
g	gram(s)
μg	microgram(s)
hr	hour(s)
i.m.	intramuscular
i.p.	intraperitoneal
IU	international unit(s)
i.v.	intravenous
kg	kilogram(s)
LD$_{50}$	median lethal dose(s)
LDH	lactic acid dehydrogenase
m	meter(s)
M	molar
mEq	milliequivalent(s)
mM	millimolar
μM	micromolar
mC,μC	milli-,microcurie(s)
mg	milligram(s)
min	minute(s)
ml	milliliter(s)
mm	millimeter(s)
MTD	maximum tolerated dose
ng	nanogram (10^{-9})
pg	picogram (10^{-12})
p.o.	orally
ppm	parts per million
r	Roentgen
RBC	red blood cells (erythrocytes), red blood count
resp.	respectively
Rev.	review (only in citations)
RNA	ribonucleic acid
s.c.	subcutaneous
sec	second(s)
SGOT	serum glutamic-oxalacetic transaminase
SGPT	serum glutamic-pyruvic transaminase
U	unit(s)
UV	ultraviolet
WBC	white blood cells (leukocytes), white blood count
yr	year(s)

NOTE

Due to circumstances beyond our control, Gastroenterology Abstracts and Citations, Volume 7, Number 4, April 1973 inadvertently was mailed to another mailing list. We have arranged for additional copies to be printed and mailed to the Gastroenterology Abstracts and Citations mailing list. This should occur in the very near future.

We regret this inconvenience to our readers, and this office will continue surveillance to make sure that this issue will be mailed out correctly as soon as possible.

PRE-CLINICAL SCIENCES

MORPHOLOGY, CELLULAR STRUCTURE AND HISTOCHEMISTRY

6129 IMMUNOLOGIC RESPONSES IN THE GASTROINTESTINAL TRACT OF THE GUINEA PIG. I. CHARACTERIZATION OF PEYER'S PATCH CELLS.

(E.) Levin, D. M.; Rosenstreich, D. L.; Reynolds, H. Y. (Natl. Inst. Allergy Infectious Dis., Bethesda, Md.). *J. Immunol.* 111(3):980-983, 1973.

Peyer's patches from 2-15 mm in length were cut from the small bowel between the stomach and the cecum of strain 13 male guinea pigs. After processing of the specimens, about 20-50 x 10^6 cells were obtained/animal. Between 2-5% of these cells had 3 or more beads. Morphologically, these bead-containing cells consisted of equal numbers of small monocytes and macrophages. The number of immunoglobulin-bearing cells in several different determinations ranged from 23-42% with a mean of 33%. Lymph node cells contained an average of 35%. Thymocytes contained 6.6%. Therefore, about 1/3 of the Peyer's patch cells appeared to be bone marrow-dependent lymphocytes. The percentage of erythrocyte-antibody-complement complex resette-forming cells ranged between 48-60%. Thus, about 1/2 the cells formed rosettes, suggesting that this group consisted of monocytes and bone marrow-dependent lymphocytes. Treatment with antithymus-dependent lymphocyte cell serum killed 90% of the thymocytes but only 5% of the leukemia cells which are bone-marrow dependent cells. Marked stimulation of the Peyer's patch cells was obtained with phytohemagglutinin (1 μg/ml) and concanavalin A (1 μg/ml), properties associated with thymus-dependent lymphocytes. Response to *E. coli* or *S. typhimurium* endotoxins (10-200 μg/ml) was small and much less than in spleen cells of the same animals, a property suggestive of bone marrow-dependent lymphocytes. These results support the secondary lymphoid role for the Peyer's patch in the adult guinea pig.

130 STUDIES ON SMALL INTESTINE ULTRASTRUCTURE IN GERMFREE FW 49 RATS. I. EPITHELIAL INDINGS WITH SPECIAL REFERENCE TO PANETH CELLS.

Ger.) Otto, H. F.; Lewerenz, I. (Pathol. Inst., niv. Hamburg, Germany). *Virchows Arch [Pathol. nat.]* 360(3):235-251, 1973.

ight and electron microscope examination of the mall intestine (duodenum, jejunum, ileum), cecum, nd ascending colon showed quantitative differences, articularly in villous height, between epithelial ells in germfree FW 49 rats and conventional rats. xaminations were performed on rats at ages 10-35 ays and at adulthood. Until the age of 21 days, hen postnatal maturation of the mucosal villi and rypts occurred, epithelial cells showed considerable asoapical differentiation. The ratio of villous eight to crypt depth was significantly greater in ermfree than in conventional rats, as was the mean eight of cells in the intestinal epithelium (40 ± at 28 days in germfree rats). Ultrastructural udies revealed expansion of the basal part of the intercellular space with close interlocking of lateral cell membranes. Desmosomes were very highly developed in the cecum and ascending colon. Most absorptive cells were found in the bottom of crypts and were associated with cecal distension or filling of the intestine with a greenish-black, viscous, meconium-like mass. Paneth cells were filled full of degenerate granules which were not expelled. These findings suggest that there is no exogenous functional stimulation of the Paneth cells. Interepithelial lymphocytes were very rarely found in comparison to eosinophilic granulocytes. No evidence was found of qualitative differences between germfree and conventional rats.

6131 MUCOSA OF THE SMALL INTESTINE AFTER LARGE DOSES OF CYCLOPHOSPHAMIDE: MORPHOLOGICAL AND HISTOCHEMICAL STUDIES IN THE GOLDEN HAMSTER.

(Ger.) Waldeck, H. H. (Anat. Inst., Univ. Tubingen, Germany). *Z. Gastroenterol.* 10(7):543-554, 1972.

Morphological changes and alkaline phosphatase activities were studied on sections from the proximal and distal small intestine taken from 24 male golden hamsters 1-96 hr after a single i.p. injection of cyclophosphamide (400 and 800 mg/kg). The first morphological changes appeared 1 hr after injection and reached a maximum, with nuclear abnormalities (clumping of chromatin, frequent pyknosis, karyorrhexis, and abnormal mitotic figures) and cytoplasmic inclusion bodies in the epithelium of the crypts and villi, after 8 hr. Both doses of cyclophosphamide caused a reduction in the distal intestine and inactivation in the proximal intestine of alkaline phosphatase activity in the apical two-thirds of the villous epithelium between 1 and 8 hr after injection. The failure of cyclophosphamide to completely inactivate alkaline phsphatase activity in the distal small intestine is attributed to the existence of different types of alkaline phosphatase. Morphological and histochemical changes in the small intestine had completely disappeared 96 hr after injection of cyclophosphamide.

6132 MORPHOLOGICAL STUDIES OF THE PANCREAS OF RATS WITH POTASSIUM DEFICIENCY WITH SPECIAL CONSIDERATION OF THE ISLETS OF LANGERHANS.

(Ger.) Burkhardt, A.; Kaess, H.; Ehlers, W. (Pathol. Inst., Univ. Heidelberg, Germany). *Virchows Arch. [Pathol. Anat.]* 360(1):57-70, 1973.

A study was made of pancreatic morphology on 10 normal male Wistar rats, 8 rats fed a diet containing less than 0.01% K and 3% Na, and 6 controls fed a K-deficient diet with 3% KCl in their drinking water. All rats were fasted for 18 hr and sacrificed 14 days after the experiment was begun. Light microscopy failed to reveal any differences between the exocrine pancreas in control and K-deficient rats. In the endocrine pancreas A-cells were decreased in size and were degranulated after fasting in controls, while in K-deficient rats the size of A-cells was slightly increased. The size and number of B-cells per islet was about the same in both groups, while the number of A-cells per islet was significantly higher in K-deficient rats (24 vs. 12 in controls). However, some of this difference may be due to difficulties in identifying and counting A-cells in controls since there was little cytoplasm and little if any cytoplasmic granulation. Many argyrophilic granules were present in the cytoplasm of A-cells in K-deficient rats. Further studies are necessary to determine whether symptoms of K deficiency may be caused by changes in glucagon synthesis or secretion.

6133 REGENERATION OF GASTRIC MUCOSA AFTER ASPIRIN-INDUCED INJURY IN THE RAT. *(E.)*

Yeomans, N. D.; St. John, D. J. B.; de Boer, W. G. R. M. (Alfred Hosp., Melbourne, Australia). *Am. J. Dig. Dis.* 18(9):773-780, 1973.

Regeneration of gastric mucosa damaged by aspirin was studied in 6-week-old male Sprague-Dawley rats, using histologic and autoradiographic technics. Aspirin (120 mg/kg) was given by esophageal intubation either in a single dose or each day for 14 days. After a single dose, 2 types of lesion were observed in the mucosa of the body of the stomach. Superficial erosions were present after 30 min and completely healed within 24 hr. Deeper erosions reached maximal numbers at 4 hr healed in an average of 5 days and were associated with a focal increase in ^{3}H-thymidine-labeled cells. The peak increase in labeling occurred between 16-48 hr. The pattern and rate of healing was not altered by repeated daily aspirin. The investigation has demonstrated slow healing of deep mucosal erosions caused by aspirin. This slow healing is explained by destruction of the progenitor zone at the time of the initial injury. Lesions in the 14-day treatment group showed evidence of both necrosis and repair and might represent either chronic erosions or the chance occurrence of an acute erosion on top of one which is recovering from earlier damage.

6134 EFFECT OF BACTERIAL FLORA ON THE MORPHOLOGY AND MUCOSAL AREA OF THE RAT SMALL INTESTINE.

(Fr.) Meslin, J. C.; Sacquet, E.; Guenet, J. L. (Natl. Ctr. Zootechnical Res., I.N.R.A., Jouy en Josas, France). *Ann. Biol. Anim. Biochim.* 13(2): 203-214, 1973.

Measurements were made of the length of the small intestine, its circumference, the mean mucosal area/unit serosal area, the mean mucosal area/cm length of the intestine, the number of villi per cm^2 of the serosa and per cm length of the small intestine, and the height of the villi in 5 germfree and 5 non-germfree male Fischer rats. The weight of the cecum was significantly greater in germfree rats, but the body weight and length of the small intestine before and after fixation were the same in both groups of rats. In germfree rats the circumference of the small intestine was decreased in the proximal third of the small intestine, the same in the middle third, and increased in the distal third, while the mucosal area was the same in the proximal third and decreased in the middle and distal regions. The number of villi was decreased in the proximal region and the same in the middle and distal regions, while the height of the villi tended to be increased in the proximal region and decreased in the other regions. No significant difference was found in the total area of the intestinal mucosa expressed as a function of body weight.

6135 CELLULAR LOCALIZATION OF THE GROUP II PEPSINOGENS IN HUMAN STOMACH AND DUODENUM BY IMMUNOFLUORESCENCE. *(E.)*

Samloff, I. M.; Liebman, W. M. (Harbor Gen. Hosp., Torrance, Calif.). *Gastroenterology* 65(1):36-42, 1973.

The localization of the group II pepsinogens in human stomach and duodenum has been investigated by immunofluorescence. The antiserum was prepared in rabbits against a preparation of group II pepsinogens which had been isolated from human seminal fluid. Parallel studies were performed with an antiserum to the group I pepsinogens. Each antiserum was found to be specific for its respective antigen by immunodiffusion. In fundic mucosa, both group I and II pepsinogens were localized to granules in the mucous neck and chief cells and both groups appeared to be present in the same granules. By immunofluorescence, group II pepsinogen was abundant in the pyloric glands of the antrum and in Brunner's glands in the duodenum. These cells did not contain group I pepsinogens. The results indicate that the human peptic cell mass is heterogeneous and that it consists of 4 types of cells The mass of cells containing group II pepsinogens is greater than that containing group I, but group II pepsinogens are not necessarily the predominant source of pepsin in gastric juice. The amounts of each group will depend on the synthesis and release from the different cell types. The finding that Brunner's glands contain and supposedly secrete pepsinogens into a milieu capable of supporting peptic activity suggests that the peptic activity of gastric juice may be augmented as it enters the duodenal bulb.

6136 AMYLOID IN THE GASTROINTESTINAL TRACT OF MICE--AN ELECTRON MICROSCOPIC STUDY. *(E.)*

Yates, R. D.; Rigdon, R. H.; Mascorro, J. A. (Tulane Univ. Sch. Med., New Orleans, La.). *Tex. Rep. Biol. Med.* 31(1):89-97, 1973.

Adult male CFW mice, 315-420 days old, were anesthetized with ether and sections of the terminal ileum were prepared for electron microscopy by fixation in 3% glutaraldehyde in cacodylate buffer. After fixation the tissues were washed in buffer, postfixed in osmium tetroxide, dehydrated through a graded series of cold ethanols, and embedded in Epon 812. Thin sections were viewed with a Philips electron microscope. Amyloid deposits consisted of long, thin unbranched and usually randomly oriented fibrils. The deposits were primarily in the connective tissue of the mucosa around the glands of Lieberkühn and adjacent to small blood vessels. In areas where the deposits were heavy, the basal lamina around the endothelial cells was completely obliterated so that the material occupied the entire subendothelial space. This apparent obstruction of the vascular spaces may affect the distribution of nutritive materials to neighboring cells, thus resulting in cytoplasmic degeneration. This study shows that the amyloid which occurs spontaneously in the ileum of old mice is identical to that observed in man and experimentally induced in animals.

6137 MORPHOMETRIC STUDIES ON THE HISTOLOGICAL BIOMORPHOSIS OF THE WALL OF THE SMALL INTESTINE.

(Ger.) Rother, P.; Walther, M.; Scheller, G.; Blume, R. (Anat. Inst., Karl Marx Univ., Leipzig, Germany). *Z. Mikrosk. Anat. Forsch.* 87(1):97-110, 1973.

Morphometric investigations were performed on the small intestines of 12 albino BD-III rats, aged 0-24 months, and 48 humans of all ages. In rats the total distance from the bottom of the crypt to the top of the villus increased from birth to 18 months. The depth of the crypt reached a maximum after 3 months, while villus height continued to increase until 18 months. In man the height of the villus increased from 0.2 mm in newborns to 0.4 mm in adults and then remained constant. In man the lamina muscularis mucosae was 20 μ thick at birth, increased to 35-40 μ at age 2 yr, and remained constant until old age. The total thickness of the tunica muscularis increased from 0.2 mm in newborns to 0.5 mm in old age. n age-dependent proliferation in connective tissue occurred only in the longitudinal layer of muscle between birth and age 50 yr. Since the extent of onnective tissue proliferation was smaller than hickening of the longitudinal muscle, muscle tissue may continue to proliferate until old age. Differ-nces between connective tissue proliferation in men nd women were not significant between ages 10 to 0 yr.

138 STUDIES ON ENDOCRINE CELLS OF THE GASTROINTESTINAL TRACT. I. HISTOTOPOGRAPHIC, LUORESCENCE MICROSCOPE, AND ULTRASTRUCTURAL STUDIES N CATS AND RATS.

(Ger.) Forssmann, W. G.; Grube, D. Anat. Inst., Univ. Heidelberg, Germany). *Z. Zellorsch. Mikrosk. Anat.* 140(4):535-550, 1973.

he location and distribution of endocrine cells ere studied in the pancreas and pyloric mucosa of ale Wistar rats and male and female cats by electron microscopy and fluorescence microscopy after exposure to formaldehyde vapors. In the cat cells with an intense yellow fluoresence, identified by electron microscopy as serotonin-containing cells, were found in the gastric glands; fluorescence occurred primarily at the basal part of the cell. Similar cells were present in the ductal epithelium, acini and, less frequently, on the periphery of islets of the pancreas. Cells with a green fluorescence throughout the entire cytoplasm were found near serotonin-containing cells in the pyloric mucosa; these are apparently gastrin cells. Green fluorescence was also present in the pancreas, particularly on the periphery of islets, and in the exocrine pancreas and duct system. In rats no evidence of serotonin-containing cells was found in the pancreas, but many cells with an intense yellow fluorescence were found in the gastrointestinal mucosa.

6139 CONTROL OF EPITHELIAL CELL PROLIFERATION IN THE SMALL INTESTINAL CRYPT.

(E.) Tutton, P. J. M. (Dept. Anat., Monash Univ., Victoria, Australia). *Cell Tissue Kinet.* 6(3):211-216, 1973.

A heat-labile factor which inhibited proliferative activity in crypt epithelium both in rat jejunum *in vivo* and in explants of rat jejunum maintained in organ culture was prepared from the soluble fraction of homogenized epithelial cells isolated from small intestinal crypts of adult male Sprague-Dawley rats. The factor appears to have tissue specificity, for it has no influence on epithelial cell proliferation in colonic crypts, esophagus, or skin. Extracts of rat intestinal villous cells prepared using identical techniques were without effect on proliferative activity of small intestinal crypt epithelium. Isoprenalin (0.3 μg/ml), which also suppressed cell proliferation in jejunal explants, did not potentiate the effect of the factor and its effects were evanescent.

6140 SMALL BOWEL ADAPTATION AFTER INTESTINAL RESECTION IN GUINEA PIG WITH FUNCTIONAL ADAPTATION OF VITAMIN B_{12} ABSORPTION.

(E.) Mackinnon, A. M. (Roy. Postgrad. Med. Sch., London, England). *Am. J. Dig. Dis.* 18(7):576-582, 1973.

The morphologic response of the ileum was examined in female jejunectomized guinea pigs. Cellular hyperplasia was demonstrated by a 2-fold increase in villous height and DNA content/unit length of ileum 8 weeks after resection. A functional response to jejunectomy was confirmed by the significantly greater than normal absorption of vitamin B_{12} (cyanocobalamin ^{58}Co; 50 ng p.o.) 5 weeks after resection. Attachment of cyanocobalamin ^{57}Co to the ileal mucosa was increased 8 weeks after operation, but uptake/milligram of mucosal DNA was decreased. The results indicate that ileal adaptation occurs after proximal resection in guinea pigs and that there is an associated increase in the capacity to absorb vitamin B_{12}.

6141 THE ISOLATION, PARTIAL CHARACTERIZATION, AND SUBFRACTIONATION OF HUMAN INTESTINAL BRUSH BORDERS. *(E.)* Houghton, S. E.; McCarthy, C. F. (Regional Hosp., Galway, Ireland). *Gut* 14(7): 529-534, 1973.

Normal specimens of the jejunum (13), duodenum (3), and ileum (4) were obtained from 20 patients (6 females and 14 males, 21-78 yr old). Operations performed at the time specimens were taken included gastrectomy and gastroenterostomy for peptic ulceration, and resections for carcinoma of the colon, ulcerative colitis, and Crohn's disease. The enzyme activities and protein content of mucosal homogenates and brush border suspensions were studied. The specific activity of sucrase in the isolated brush borders was 6.5 times that in the original mucosal homogenate. Activities of lactase and alkaline phosphatase increased 4 and 8 times, resp. No significant differences were noted in enzyme activity among the duodenal, jejunal, and ileal segments. The presence of papain (11.0 mg/ml) during the incubation of the brush borders had no effect on the activity of the 3 enzymes. These results indicate that human brush borders can be isolated as pure and undamaged as those from other species. All 3 enzymes studied appeared localized in the microvilli of the human intestine, as is true for other species. The fact that the disaccharidase activity of the human brush borders can be isolated in a particulate fraction shows a further similarity with other species. In comparing hamster and human brush borders, the distribution of alkaline phosphatase is the same.

6142 GEOGRAPHICAL VARIATIONS IN THE MORPHOLOGY OF THE SMALL INTESTINAL MUCOSA IN APPARENTLY HEALTHY INDIVIDUALS. *(E.)* Baker, S. J. (Christian Med. Coll. Hosp., Vellore, Tamilnadu, India). *Pathol. Microbiol. (Basel)* 39(3/4):222-237, 1973.

To determine what different workers consider to be "normal" intestinal biopsy findings, macroscopic, and microscopic photographs of 7 jejunal biopsies illustrating the range of morphological changes found in southern Indian control subjects were circulated, together with a questionnaire, to observers in different parts of the world. There was general agreement among the observers regarding the "normality" of the biopsy showing the least changes and the abnormality of the 2 showing the most marked changes. However, there was considerable disagreement over those intermediate between these extremes. A few observers considered some appearances normal in the tropics but abnormal in temperate regions, indicating their concept of normality was influenced by prevalence. Opinion regarding the prevalence of the different biopsy appearances in control subjects varied significantly between temperate and tropical areas. It is suggested that intestinal parasitism, environmental contamination, and malnutrition are important factors in the etiology of biopsy abnormalities in apparently healthy tropical residents. Bacterial contamination, viruses, and other factors are possibly involved, but the evidence is inconclusive. Whatever the specific factors are, the fact that these abnormalities regress when the subject moves to the temperate zone, suggests that the damaging agent is active in the tropical climate.

6143 ULTRASTRUCTURAL ALTERATIONS IN ISCHAEMIC LESION OF SMALL INTESTINAL MUCOSA IN EXPERIMENTAL SUPERIOR MESENTERIC ARTERY OCCLUSION. *(E.)* Aho, A. J.; Arstila, A. U.; Ahonen, J.; Inberg, M. V.; Scheinin, T. M. (Dept. Surg., Univ. Turku, Finland). *Scand. J. Gastroenterol.* 8(5):439-447, 1973.

Ultrastructural changes in canine small bowel mucosal cells produced by superior mesenteric arterial occlusion were studied in sequential biopsies taken before and 15 min to 5 hr after the occlusion. The effects of breathing air and oxygen during arterial occlusion were compared. During air breathing, occasional changes in cellular ultrastructure occurred only after 30 min of occlusion. Mitochondrial changes, clumping of nuclear chromatin, and dilatation of endoplasmic reticulum were some of the first signs of damage. Later, breakage of microvilli and swelling of mitochondria occurred. The changes were not uniform from cell to cell, and apparently normal cells were observed among damaged ones. After 2 hr, junctional complexes between many cells broadened, through cell membrane disruption, cells tended to detach from each other and changes in intracellular organelles progressed. Clearly lethal changes first became apparent in places after 4 hr of arterial occlusion. The morphological changes corresponded to the expected biochemical enzyme changes, except for the early increase in LDH activity in the thoracic duct lymph. Breathing of pure oxygen protected the intestinal mucosal cells during arterial occlusion, although dilatation of rough endoplasmic reticulum, as an isolated change, was observed fairly early. It is suggested that oxygen may counteract the effect of circulatory endotoxins which have been observed by some investigators.

6144 A HISTOCHEMICAL STUDY OF THE INCLUSION BODIES IN THE SMALL INTESTINE OF THE DEVELOPING RAT. *(E.)* Shervey, P. D. (Univ. Nebraska, Coll. Med., Omaha). *Z. Anat. Entwicklungegesch.* 141(1):39-53, 1973.

The morphology and histochemistry of the epithelium in the small intestine was studied in the fetal and suckling rat. Large supranuclear inclusion bodies in the ileum of the suckling animal gave positive reactions for the following components and enzymes: lipofuscins; amino and SH groups; 1-2 glycols; alkaline phosphatase; acid phosphatase; and nonspecific esterase. Alcian blue left these bodies unstained and no leucine aminopeptidase activity was noted. Small periodic acid-Schiff-positive droplets and unstained vacuoles formed in the supranuclear cytoplasm during terminal gestation. The droplets enlarged rapidly and formed the large supranuclear inclusions during the first 24-48 hr postpartum. However, high levels of enzyme activity did not occur in the large inclusions until 2-4 days after birth. This may be related to the levels of enzyme production and/or accumulation within the columnar cell.

6145 PANCREATIC MORPHOLOGY. A COMBINED RADIOLOGICAL AND PATHOLOGICAL STUDY. *(E.)* Kreel, L.; Sandin, B.; Slavin, G. (Clin. Res. Ctr., Northwick Park, Harrow, England). *Clin. Radiol.* 24:154-161, 1973.

To determine normal variations in pancreatic morphology, post mortem retrograde pancreatography was attempted in 80 instances (41 males and 39 females, most over 70 yr of age) and was carried out successfully in 77. A study of the *in situ* morphology revealed a great variation in size, shape, and position of the pancreas and its ducts. Moreover, filling defects due to normal structures such as the superior mesenteric and splenic arteries were demonstrated. An accessory duct was present in 19 instances. In 18 the accessory papilla lay above the papilla of Vater and in 1 case, below. This causes difficulty during *in vivo* examination of the pancreatic duct since the contrast medium leaks out of the accessory papilla. Greater difficulty occurs when the pancreatic duct opens completely separately from the common bile duct; in these cases the papilla is not visible to indicate the site of the pancreatic duct. Unsuspected malignant tumors were detected by this method and appeared to be a not uncommon finding. Ductular ectasia was also commonly noted. Although a minor papilla had previously been described as being present in all cases, in the present study an accessory duct opening on the minor papilla was found in only 24% of cases.

6146 PATHOLOGIC CHANGES IN THE GASTRODUODENAL MUCOSA AFTER INFRA-ARTERIAL INFUSION OF 5-FLUOROURACIL. *(E.)* Athanassiades, S.; Deligeorge, H.; Kalachanis, N.; Paraskevas, G. (Areteion Hosp., Athens, Greece). *Am. J. Surg.* 126(3):319-321, 1973.

Infusion of 5-fluorouracil in the left gastric artery of dogs damaged the gastric mucosa. Lesions varied from superficial necrosis to ulcers that had the histologic characteristics of chronic gastric ulcer. One group of dogs received 3 mg/kg 5-fluorouracil in 20 cc of normal saline through the catheter in a slow 10 min infusion. A second group received 5 mg/kg in the same manner. A third group received 3 mg/kg for 5 succeeding days and then every other day for a total of 10 infusions in a week period. The most severe lesions occurred in ogs with prolonged infusion, whereas dogs infused with approximately the same total dose over a short period developed necrosis of gastric epithelium but no ulceration. These findings suggest that the ulcerogenic action of 5-fluorouracil results from its effect on the rate of exfoliation and the rate of renewal of gastric mucosal cells. It is also possible that superficial epithelial necrosis which occurs initially makes the mucosa susceptible to the highly acidic gastric juice. Upper gastrointestinal bleeding in patients given 5-fluorouracil infusions in the hepatic artery in those with a normal platelet counts could be caused by peptic ulcer, rather than by bone marrow depression and thrombocytopenia, and thus should be treated surgically.

6147 ULTRASTRUCTURE OF PEYER'S PATCHES IN THE AGED MOUSE. *(E.)* Chin, K. N. (Fac. Med., Univ. Sheffield, England). *Acta Anat.* 84(4):523-533, 1973.

An electron microscopic study was carried out on the effects of age on the Peyer's patches of the normal mouse. Most of the age-related changes were seen in the stroma and the reticular cells rather than in the lymphoid components of the patch. No atrophy, fibrosis or adipose tissue invasion was observed in the aged patch, but there was a deposition of elastin-like material alongside the collagen septa. In comparison with younger animals, a more prominent collection of intracytoplasmic fibrils in the reticular cells was evident in older mice. More collagen fibrils were in apposition to the external surface of the cell; few lysosomes were present in the cytoplasm of the reticular cell. Very few plasma cells and granulocytes were seen. What may have been remains of mast cells were observed in the macrophages. Intact mast cells were not observed. Some macrophages showed lipofuscin granules and clear vacuoles in their cytoplasm. Large binucleate reticular cells were newly encountered. Nonmyelinated nerve fibers and a rare ganglion cell were seen at the periphery of the patch just below the intestinal epithelium.

6148 LIVER FUNCTION AND HISTOLOGY IN VARIOUS SPECIES OF ANIMAL TREATED WITH NON-LETHAL DOSES OF AFLATOXIN B_1. *(E.)* Bassir, O.; Bababunmi, E. A. (Dept. Biochem., Univ. Ibadan, Nigeria). *J. Pathol.* 108(1):85-90, 1973.

Pure aflatoxin B_1 (58 μg/kg, i.p.) was given to goats, Wistar albino rats, and Muscovy ducks. Other animals of these same species received carbon tetrachloride (3 ml/kg, i.p.). Indocyanine green (5 mg/kg) was injected 3 hr after the aflatoxin B_1 or 72 hr after the carbon tetrachloride. The clearance rate for indocyanine green in animals receiving aflatoxin B_1 was not significantly different from control values. In animals receiving carbon tetrachloride, the levels were significantly diminished, e.g., from 2.8 to 0.6 mg/100 ml plasma/min in rats. All 3 species receiving aflatoxin B_1 showed significant increases in blood clotting time, e.g., the mean normal thrombotest time increased from 28.5 to 41.2 sec for rats.

Carbon tetrachloride caused no coagulation defect. Histological examination of livers revealed none of the previously reported and expected pathological changes. Treated ducks did not show the fatty infiltration characteristic of aflatoxin carcinogenesis in the duck. It is concluded that the hemorrhagic effect of aflatoxin B_1 is likely due to specific inhibition of prothrombin synthesis by competition for the apoenzyme, rather than to any generalized hepatocellular damage, since indocyanine green is removed from the plasma entirely by the liver and is not recirculated.

6149 LOCALIZATION OF INTRACELLULAR IMMUNOGLOBULIN A IN PORCINE INTESTINAL MUCOSA USING ENZYME-LABELLED ANTIBODY. AN ULTRASTRUCTURAL STUDY.

(E.) Allen, W. D.; Smith, C. G.; Porter, P. (Unilever Res. Lab., Sharnbrook, England). *Immunology* 25(1):55-70, 1973.

Immuno-electron microscopy and immunofluorescence were used to study the intracellular localization of IgA in porcine intestinal tissue. IgA was demonstrated in many vesicles occurring in the cytoplasm of crypt epithelial cells and in the intracellular spaces. Also, on one occasion, a vessel was observed as it appeared to cross an epithelial cell membrane. IgA was also shown in the ergastoplasmic cisternae of plasma cells in the intercryptal lamina propria. For most of their length, the intercellular spaces are about 20-30 nm wide and are sealed at their apices by the zona occludens where cell membranes of adjacent columnar cells are in close apposition. Direct passage of macromolecules between the intercellular space and the lumenal surface is prevented by this junction. The concept of a pathway, similar to pinocytosis, by which secretory IgA may pass from the intercellular space into the cytoplasm of the epithelial cell and from there through the brush border into the lumen is suggested. Thus, vessels containing IgA pass through the epithelial cell cytoplasm, accumulate in the supranuclear region, and are then passed into the intestinal lumen by apocrine or merocrine excretion. This concept is supported by the relatively large amounts of IgA found in exocrine secretions compared with very little found in the circulation.

6150 MICROVASCULAR CHANGES OF GASTRIC MUCOSA IN THE DEVELOPMENT OF STRESS ULCER IN RATS.

(E.) Hase, T.; Moss, B. J. (Walter Reed Army Inst. Res., Washington, D.C.). *Gastroenterology* 65(2): 224-234, 1973.

In normal and rotationally stressed rats, gastric mucosal microvascular patterns were studied by India ink injection and silicone rubber perfusion techniques. In normal rats, the mucosal microvascular pattern was characterized by a capillary network which enclosed the gastric glands and spanned the distance between the connecting arterioles at the base of the mucosa and the tips of connecting venules at the surface of the mucosa. Submucosal arteriovenous anastomoses, from 20-40 μ in size, were demonstrated. In the stressed rats, ischemic change of the mucosa, which was initially general but becomes focal later, was found. This study indicates that in stress, mucosal ischemia is caused by contraction of connecting arterioles, and that persistent, focal ischemia of the gastric mucosa triggers tissue damage and development of stress ulcer. Therefore, stress in itself can cause focal ischemia and erosion of gastric mucosa. It is suggested that these stress-induced changes be considered in determining the pathogenesis of human gastric ulcers.

6151 CYTOCHEMICAL AND ULTRASTRUCTURAL ALTERATIONS ASSOCIATED WITH CONFLUENT GROWTH IN CELL CULTURES OF EPITHELIAL-LIKE CELLS FROM RAT LIVER.

(E.) Williams, G. M.; Stromberg, K.; Kroes, R. (Natl. Cancer Inst., Bethesda, Md.). *Lab. Invest.* 29(3):293-303, 1973.

Epithelial-like cell cultures from rat liver were studied in the confluent state to determine if they were functionally more active than in the preconfluent state. Studies of the cytochemical activities of 13 enzymes and the ultrastructure of the cells were performed on cells in postconfluent cultures. The activities of 5 of the 12 cell enzymes were greater in confluent cultures. By displaying a large increase on cytoplasmic 75-A fibrils the that of preconfluent cells. In postconfluent cultures the amount of free polyribosomes were reduced and in some cells microbodies were more numerous. In the preconfluent and newly confluent state, the growth fraction was 1.0. The growth fraction decreased only when cultures were maintained postconfluency. It is concluded that phenotypic modulation occurs in confluent cultures before a decrease in growth fraction, but that further modulation occurs when the degree of cell proliferation is reduced.

6152 RADIATION AND ACTINOMYCIN D MORTALITY STUDIES IN C57BL/6 MICE. II. COMBINED TREATMENT AND GASTROINTESTINAL LETHALITY. *(E.)*

Concannon, J. P.; Dalbow, M. H.; Hagemann, R. F.; Frich, J. C.; Hodgson, S. E.; Weil, C. S.; Martinelli, R. (Allegheny Gen. Hosp., Pittsburgh, Pa.). *Cancer* 32(3):553-561, 1973.

C57BL/6 mice were treated with actinomycin (770, 1156, or 1730 μg/kg) or radiation therapy (957, 1100, 1265, or 1455 R) or with a combination of the 2 agents. LD_{50} estimates based on radiation doses were calculated from 6-day (intestinal death) mortality data. To determine the main effects for actinomycin or radiation exposure as well as actinomycin-radiation interactions, a factorial analysis of the data was performed. The LD_{50} data indicated that the combined treatment was generally more lethal in causing intestinal death than either agent given independently. Significant main effects for actinomycin and radiation were generally observed with few actinomycin-radiation interactions. The principal mechanism for intestinal death in animals treated with various combinations of actinomycin and radiation exposure was additive cytotoxicity at the level of crypt survival and/or prolongation of the time to the appearance of the compensatory proliferative response.

6153 STUDIES OF THE ENDOCRINE CELLS OF THE GASTROINTESTINAL TRACT. II. FLUORESCENCE MICROSCOPY OF EC CELLS WITH A TRYPTOPHAN-FREE DIET. *(Ger.)* Grube, D.; Forssmann, W. G. (Anat. Inst., Univ. Heidelberg, Germany). *Z. Zellforsch. Mikrosk. Anat.* 140(4):551-565, 1973.

Serotonin-containing cells were studied in the pylorus and duodenum of male Wistar rats fed balanced and tryptophan-free diets. Tissue was exposed to formaldehyde vapors for 1-3 hr before examination under the fluorescence microscope. In controls fed balanced diets, serotonin-containing cells, identified by their intense yellow fluorescence, were present in almost equal numbers in the surface and glandular epithelium of the duodenum, while about 75% were present in the glandular epithelium in the pylorus. A large decrease occurred in the number of serotonin-containing cells and in the intensity of their fluorescence in both the pylorus and duodenum of rats fed a tryptophan-free diet. In the duodenum the number of serotonin-containing cells decreased to 66% of the control value after 27 days and to 55% after 41 days on the tryptophan-free diet; this decrease was most pronounced in the glandular epithelium. In the pylorus the number of serotonin-containing cells decreased to 57% of the control value after 27 days and to 30% after 41 days on the tryptophan-free diet; this decrease was most marked in the surface epithelium. When rats fed the tryptophan-free diet for 27 days were given a balanced diet, rapid clinical improvement was accompanied by a significant increase in the number of serotonin-containing cells after 7 days. In the duodenum this increase was particularly evident in the glandular epithelium and in the pylorus, in the surface epithelium. These findings suggest that serotonin metabolism occurs primarily in the glandular epithelium in the duodenum and in the surface epithelium in the pylorus. Serotonin is both synthesized and stored in serotonin-containing cells of the stomach and duodenum.

6154 THE INDUCTION OF FIBRILLAR NUCLEOLI IN RAT LIVER CELLS BY D-GALACTOSAMINE AND THEIR SUBSEQUENT RE-FORMATION INTO NORMAL NUCLEOLI. *(E.)* Shinozuka, H.; Martin, J. T.; Farber, J. L. (Temple Univ. Sch. Med., Philadelphia, Pa.). *J. Ultrastruct. Res.* 44(3-4):279-292, 1973.

Changes in the fine structure of rat liver cell nucleoli after a single injection of D-galactosamine (100, 200, or 400 mg/kg, i.p.) were investigated. At all dosages galactosamine induced extensive fragmentation of nucleoli within 2 hr. Subsequently, these fragments disappeared and small, spherical, fibrillar bodies appeared. The altered nucleoli begin to re-form a normal structure between 12 and 24 hr. This reforming involved the fibrillar nucleoli with the appearance of granular material and the formation of small rod-like nucleolonema. The administration of uridine (1.2 mg/g) simultaneously with galactosamine completely protected against nucleolar alterations. Uridine also reversed the galactosamine-induced lesions when given several hours after the galactosamine. These results suggest that the galactosamine-induced disturbance of RNA metabolism and the accompanying nucleolar fragmentation is mediated by the intracellular deficiency of uridine nucleotides. Fibrillar nucleoli like those induced by galactosamine may represent a common morphological manifestation of the absence of ribosomal RNA synthesis.

6155 STUDIES ON THE EFFECT OF MECHANICAL VIBRATIONS ON THE CELLS OF PARENCHYMAL ORGANS IN TISSULAR CULTURES. BEHAVIOR OF THE LIVER CELLS MITOTIC CYCLE IN CHICK EMBRYOS. *(E.)* Kwolek, A.; Kuleta, E. (Silesian Med. Acad., Zabrze, Poland). *Acta Physiol. Pol.* 23(4):697-703, 1972.

6156 STRUCTURAL AND FUNCTIONAL CHANGES IN LIVER MITOCHONDRIA OF MICE FED PALMITOYLETHANOLAMIDE (PEA). *(E.)* Obermajerova, H.; Masek, K.; Seifert, J.; Buchar, E.; Havlik, I. (Inst. Pharmacol., Czechoslovak Acad. Sci., Prague). *Biochem. Pharmacol.* 22(20):2529-2536, 1973.

6157 CRYSTALLINE STRUCTURES IN THE HYALOPLASM OF HUMAN LIVER CELLS. *(E.)* Kovacs, K.; Horvath, E.; Lee, R.; Little, J. A. (St. Michael's Hosp., Univ. Toronto, Canada). *Acta Hepatogastroenterol.* 20(4):294-298, 1973.

6158 ACTION OF EXOGENOUS THYMIDINE IN VIVO ON PROGENITOR CELL CYCLE IN INTESTINAL EPITHELIUM. *(E.)* Sawicki, W.; Dorn, A. (Sch. Med., Warsaw, Poland). *Acta Histochem.* 46:181-185, 1973.

6159 AN INTRACRYSTAL STRUCTURE IN RAT LIVER DUMBBELL-SHAPPED MITOCHONDRIA. PRELIMINARY COMMUNICATIONS. *(E.)* Chaldakov, G. N.; Kokosharov, P. N. (Med. High Sch. Varna, Bulgaria). *Acta Morphol. Acad. Sci. Hung.* 21(2):149-154, 1973.

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6161 SYNCHRONIZATION OF BABY RAT HEPATOCYTES: A NEW TEST FOR THE DETECTION OF FACTORS CONTROLLING DNA SYNTHESIS IN RAT HEPATIC CELLS. *(E.)* Nadal, C. (Cellular Physiol. Unit, I.N.S.E.R.M., Radium Inst., Orsay, France). *Cell Tissue Kinet.* 6(5):437-446, 1973.

6162 DISTRIBUTION OF INSULIN RECEPTOR SITES AMONG LIVER PLASMA MEMBRANE SUBFRACTIONS. *(E.)* Evans, W. H.; Bergeron, J. J. M.; Geschwind, I. I. (Natl. Inst. Med. Res., London, England). *F.E.B.S. Lett.* 34(2):259-262, 1973.

6163 QUANTITATION OF ACID PHOSPHATASE AND ARYL SULPHATASE IN RAT HEPATIC PARENCHYMAL AND KUPFFER CELLS. *(E.)* Arborgh, B.; Berg, T.; Ericsson, J. L. E. (Sabbatsberg's Hosp., Stockholm, Sweden). *F.E.B.S. Lett.* 35(1):51-53, 1973.

6164 ON THE IN VITRO BEHAVIOUR OF MOUSE SUB-MAXILLARYGLAND CELLS. *(E.)* Marcante, M. L. (Regina Elena Inst. Cancer Res., Rome, Italy). *J. Cell Sci.* 13(2):441-445, 1973.

6165 A RAPIDLY SEDIMENTING FRACTION OF RAT LIVER ENDOPLASMIC RETICULUM. *(E.)* Lewis, J. A.; Tata, J. R. (Natl. Inst. Med. Res., London, England). *J. Cell Sci.* 13(2):447-459, 1973.

6166 ANASTOMOSIS OF TRANSPLANTED FETAL RAT INTESTINE TO THE NORMAL INTESTINE OF THE HOST. *(E.)* Deutsch, A. A.; Leapman, S. B.; Arensman, R.; Folkman, J. (Children's Hosp. Med. Ctr., Boston, Mass.). *J. Surg. Res.* 15(3):176-181, 1973.

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6171 INTERCELLULAR CONTACTS AT THE EPITHELIAL-MESENCHYMAL INTERFACE DURING THE PRENATAL DEVELOPMENT OF THE RAT SUBMANDIBULAR GLAND. *(E.)* Cutler, L. S.; Chaudhry, A. P. (Sch. Med., State Univ. New York, Buffalo). *Dev. Biol.* 33(2):229-240, 1973.

6172 PROGRESS IN MEASURING EPITHELIAL TURN-OVER IN THE VILLUS OF THE SMALL INTESTINE. *(E.)* Clarke, R. M. (Dept. Human Morphology, Univ. Nottingham, England). *Digestion* 8(2):161-175, 1973.

6173 DEVELOPMENTAL STUDIES OF THE HUMAN GALL-BLADDER EPITHELIUM. *(Jap.)* Miki, S. (Sch. Med., Tokushima Univ., Japan). *Shikoku Acta Med.* 29(3):270-286, 1973.

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6176 BLEOMYCINE-INDUCED CHANGES IN CYTOKINESIS OF THE MUCOSA OF THE SMALL INTESTINE. *(Ger.)* Burkle, G.; Buhler, B.; Dietz, J.; Burkle, V. (no affil.). *Virchows Arch. (Pathol. Anat.)* 360(3):209-222, 1973.

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6182 DIFFERENTIATION OF THE MYOEPITHELIAL CELLS OF THE RAT SUBMANDIBULAR GLAND IN VIVO AND IN VITRO: AN ULTRASTRUCTURAL STUDY. *(E.)* Cutler, L. S.; Chaudhry, A. P. (Sch. Med., State Univ. New York, Buffalo). *J. Morphol.* 140(3):343-354, 1973.

6183 EFFECT OF 5-HYDROXYTRYPTOPHAN ON THE DIFFERENTIATION OF ARGYROPHIL TO ARGENTAFFIN CELLS IN THE INTESTINE OF THE GUINEA-PIG AFTER PRETREATMENT WITH IPRONIAZID AND RESERPINE. *(E.)* Kazzaz, B. A. (Dept. Pathol., Manchester Univ., England). *J. Pathol.* 110:75-82, 1973.

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6207 PANCREATIC-TYPE TISSUE IN LIVERS OF RATS FED POLYCHLORINATED BIPHENYLS. *(E.)* Kimbrough, R. D. (Environ. Prot. Agency, Chamblee, Ga.). *J. Natl. Cancer Inst.* 51(2):679-681, 1973.

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6210 DESCRIPTION OF STRUCTURES ANALOGOUS TO ANNULATE LAMELLAE IN NORMAL AND PATHOLOGICAL CELLS OF THE EXOCRINE PANCREAS IN MAN AND THE RAT. *(Fr.)* Lechene-de la Porte, P. (Unit. Gastrointestinal Pathol., Marseille, France). *C. R. Acad. Sci. (Paris)* 276(8):2549-2552, 1973.

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MORPHOLOGY, CELLULAR STRUCTURE AND HISTOCHEMISTRY

6234 EXPERIMENTAL HISTOCHEMICAL INVESTIGATION OF THE CONDITION OF GASTRIC GLANDS DEPENDING UPON THE CHARACTER OF ALIMENTATION AND AGE. *(Rus.)* Smolyansky, B. L.; Zhukova, N. M. (Leningrad Med. Inst. Sanitation Hyg., USSR). *Vopr. Pitan.* (3): 30-33, 1973.

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See also, 6264, 6266, 6274, 6361, 6363, 6400, 6408, 6426, 6439, 6579, 6602, 6690, 6995, 7034, 7373, 7692, 7856.

ABSORPTION—EXCRETION—TRANSPORT

6236 VITAMIN D AND INTESTINAL CALCIUM FLUXES IN VIVO IN THE RAT. *(E.)* Younoszai, M. K.; Urban, E.; Schedl, H. P. (Univ. Iowa Coll. Med., Iowa City). *Am. J. Physiol.* 225(2):287-292, 1973.

The effects of vitamin D on flux of calcium into the intestinal lumen were measured. Vitamin D-depleted and -repleted male albino Carworth rats were injected parenterally with ^{45}Ca and its entry into the lumen was measured under steady-state conditions during luminal perfusion of calcium-free and calcium-containing (^{40}Ca) solutions. Net calcium movements were measured during perfusion of both calcium-free and calcium-containing solutions. Plasma-to-lumen flux of calcium was calculated from entry rate of ^{45}Ca into the lumen, and lumen-to-plasma flux of calcium was calculated as the sum of net absorption and plasma-to-lumen flux. There was net absorption of ^{40}Ca and secretion of ^{45}Ca during luminal perfusion with ^{40}Ca. There was net secretion of both ^{40}Ca and ^{45}Ca during luminal perfusion with calcium-free solutions. Vitamin D increased net absorption and lumen-to-plasma flux of calcium in duodenum but not in ileum. Secretion rate of calcium in ileum was twice that in duodenum. Vitamin D had no effect on net secretion or plasma-to-lumen flux of calcium in either duodenum or ileum. Thus, vitamin D had a directionally oriented action on transmucosal calcium transport: it increased lumen-to-plasma but not plasma-to-lumen flux. Therefore, the net effect of vitamin D cannot be explained by the increase in passive permeability of the mucosa.

6237 INTESTINAL TRANSPORT OF ANTIBODIES IN THE NEWBORN RAT. *(E.)* Rodewald, R. (Sch. Med., Univ. Pennsylvania, Philadelphia). *J. Cell Biol.* 58(1):189-211, 1973.

The mophology of the absorptive epithelial cells in the proximal small intestine of the neonatal rat was studied together with the transport across these cells of several immunoglobulin tracers: ferritin-conjugated immunoglobulins and antiperoxidase antibodies. Cells exposed to rat ferritin-conjugated IgG bound the tracer on the membrane of tubular invaginations of the apical cell surface. Tubular and coated vesicles within the cell also contained the tracer, as did the intercellular spaces. Uptake of tracer was highly selective and occurred only with rat or cow ferritin-conjugated IgG. When cells were exposed to chicken ferritin-conjugated IgG, ferritin-conjugated bovine serum albumin, or free ferritin, tracer did not enter the cell or appear in the intercellular spaces. A similar selective uptake and transport of only the homologous antibody was seen in experiments with rat and chicken antiperoxidase. When cells from the distal small intestine were exposed to the tracers, all tracers were absorbed nonselectively but none were released from the cells. Cells from the proximal small intestine of the 22-day-old rat failed to absorb even rat ferritin-conjugated IgG. A model is presented for selective antibody transport in proximal cells of the neonatal rat in which antibodies are selectively absorbed at the apical cell surface by pinocytosis within tubular vesicles. The antibodies are then transferred to the intercellular space within coated vesicles. Distal cells function only to digest proteins nonselectively.

6238 SODIUM AND WATER TRANSPORT ACROSS THE JEJUNUM OF FASTED RATS. *(E.)* Beck, I. T.;

Dinda, P. K. (Hotel Dieu Hosp., Kingston, Ontario, Canada). *Can. J. Physiol. Pharmacol.* 51(6): 05-409, 1973.

The effect of 72 hr fasting on the transmural electrical potential difference, the unidirectional fluxes, and the net flux of sodium and the net transport of fluid across the jejunum of female albino Wistar rats was investigated. Everted jejunal segments were incubated in 12 ml of Krebs-Ringer bicarbonate solution containing 5.55 mM glucose on either side for 1 hr at 37 C. After a 72 hr fast, a 63% increase in the transmural potential difference, a 60% increase in the flux of Na from the mucosal to the serosal side, and a 48% increase in the flux of Na from the serosal to the mucosal side were noted. The net mucosal to serosal Na flux increased by 97%. There was also a 41% increase in fluid transport across the intestine of fasted rats. The concomitant increase in Na and fluid transport and in transmural potential difference is consistent with the current hypotheses of fluid and Na transport.

6239 INDEPENDENT JEJUNAL MECHANISMS FOR GLYCINE AND GLYCYLGLYCINE TRANSFER IN MAN IN VIVO.

(E.) Cook, G. C. (Dept. Med., Univ. Zambia, Lusaka). *Br. J. Nutr.* 30(1):13-19, 1973.

Rates of absorption of glycine and glycylglycine from a 300 mm jejunal segment were compared *in vivo* when the compounds were given alone or together to 6 Zambian African subjects (aged 21-58 yr) with no clinical evidence of malnutrition or gastrointestinal disease. Solutions containing glycine (100 mmol/liter), glycine (100 mmol/liter) + glycylglycine (50 mmol/liter), or glycylglycine (50 mmol/liter) were infused into the upper jejunum by means of a double-lumen tube perfusion system. The rate of glycine absorption was significantly higher from the solution containing only glycylglycine than from the glycine solution. The glycine absorption rate from the glycine + glycylglycine solution was very similar to the sum of the absorption rates of glycine from the other two substances. The luminal disappearance rate of glycylglycine from its solutions was similar in all subjects; the rate was significantly greater than the total glycine absorption rate from glycylglycine solution and indicates back-diffusion of glycine into the lumen after glycylglycine hydrolysis. The results indicate that *in vivo* transport mechanisms for glycine and glycylglycine in man are largely, if not wholly, separate.

6240 EFFECT OF ESCHERICHIA COLI ON FLUID TRANSPORT ACROSS CANINE SMALL BOWEL. MECHANISM AND IME-COURSE WITH ENTEROTOXIN AND WHOLE BACTERIAL CELLS.

E.) Guerrant, R. L.; Ganguly, U.; Casper, A. G. T.; oore, E. J.; Pierce, N. F.; Carpenter, C. C. J. (Bal-imore City Hosp., Md.). *J. Clin. Invest.* 52(7):1707-714, 1973.

An *Escherichia coli* strain isolated from a patient with severe cholera-like diarrhea produced a partly heat-labile enterotoxin shown to cause prompt adenyl cyclase stimulation and isotonic fluid secretion in canine jejunum. Both responses disappeared upon removal of the enterotoxin. The duration of action of a submaximal dose of this *E. coli* enterotoxin was brief, despite sustained exposure to the jejunum, suggesting inactivation of the enterotoxin by its interaction with the mucosa. Inoculation of whole bacterial cultures of this *E. coli* strain into canine duodenum was followed by bacterial survival and induction of net secretion after 4-7 hr. The onset of fluid production was associated with increasing mucosal adenyl cyclase activity in the intestine. Washed bacterial cells could also produce fluid secretion. When duodenal segments were challenged with viable *E. coli* of a control strain isolated from a convalescent cholera patient, slight net secretion but no adenyl cyclase activation occurred during the 7 hr observation period. This suggests that pathways other than adenyl cyclase activation by enterotoxin may be of importance in intestinal secretion caused by viable bacteria. Multiplication of the enterotoxin-producing *E. coli* was demonstrated *in vivo* 6-12 hr after intraduodenal inoculation of approximately 10^6 organisms. This was associated with fluid secretion. No evidence of histopathologic change or tissue invasion was noted, suggesting that the secretory process is enterotoxin-mediated and does not cause structural damage visible on light microscopy.

6241 DIFFERENTIAL ACTION OF PARATHYROID AND THYROID HORMONES ON EFFECTIVE INTESTINAL ABSORPTION OF CALCIUM. IN VIVO STUDIES WITH ^{47}CALCIUM RATS.

(E.) Hehrmann, R.; Hagemann, J.; Montz, R.; Jentsch, E. (Dept. Nucl. Med., Univ. Hamburg, Germany). *Acta Endocrinol (Kbh.)* 73(3): 489-498, 1973.

The actions of parathyroid extract, dibutyryl cyclic AMP, calcitonin, and thyroid extract (thyreoidea sicca) on effective intestinal calcium absorption in intact parathyroidectomized rats, and radio-thyroidectomized rats were evaluated by a new, physiological *in vivo* method. Animals were killed 10 hr after the administration of ^{47}calcium labelled food and the entire intestine was removed. Whole body retention of ^{47}calcium was measured, allowing the calculation of the effective intestinal absorption of calcium. The known actions of parathyroid extract and dibutyryl cyclic AMP monophosphate were confirmed by this method. Calcitonin did not exert a direct effect on any of the experimental groups. The absence of thyroid hormones remarkably reduced effective calcium absorption. In the presence of endogenous parathyroid hormone, the administration of minimal amounts of thyroid hormones was sufficient to increase effective calcium absorption, whereas parathyroid extract and dibutyryl cyclic AMP monophosphate did not have any effect. In the absence of parathyroid hormone, thyroid hormones did not enhance effective absorption, suggesting that thyroid hormones alone do not stimulate the effective absorption of calcium. It is concluded that the thyroid hormones act indirectly, as a permissive agent, enabling parathyroid hormone to exert its active stimulating effect on the effective intestinal absorption of calcium.

6242 USE OF INERT GASES TO STUDY THE INTERACTION OF BLOOD FLOW AND DIFFUSION DURING PASSIVE ABSORPTION FROM THE GASTROINTESTINAL TRACT OF THE RAT. *(E.)* Levitt, M. D.; Levitt, D. G. (Dept. Med., Univ. Minnesota, Minneapolis). *J. Clin. Invest.* 52(8)1852-1862, 1973.

Measurement of the relative absorption rates of inert gases (hydrogen, methane, helium, sulfur hexafluoride, and xenon-133) was used to investigate the interaction between diffusion and blood flow during passive absorption from the stomach, small bowel, and colon of the rat. The absorption data were fitted to a series of models of interaction between perfusion and diffusion. A simple model accurately predicted the absorption rates of the gases from all segments of bowel. In this model, gas is absorbed into two distinct blood flows: one which flows in proximity to the lumen and completely equilibrates with the lumen, and a second which is sufficiently rapid and distant from the lumen that its gas uptake is entirely diffusion limited. The fraction of the total absorption attributable to the equilibrating flow can be readily calculated and equalled 93%, 77%, and 33% for the small bowel, colon, and stomach, resp. Thus the rate of passive absorption of gases from the small bowel is limited by the diffusion rate of the gases. The flow which equilibrates with the lumen can be quantitated, and this flow may be a useful measure of "effective" mucosal blood flow.

6243 INTESTINAL ABSORPTION OF SODIUM AND POTASSIUM FROM ISOTONIC SOLUTIONS: A STUDY BY THE PERFUSION TECHNIQUE IN MAN. *(Fr.)* Rambaud, J. C.; Thiry, C.; Bernier, J. J. (St. Lazare Hosp., Paris, France). *Acta Gastroenterol. Belg.* 36:9-29, 1973.

Intestinal perfusion studies with isotonic solutions of sodium chloride and potassium chloride were carried out at a constant rate of 8 ml/min in 30 healthy subjects. The Na and K concentrations were reciprocally varied to assess the effect of these variations on net and unidirectional Na and K fluxes in a 25 cm test segment. In jejunum, the luminal concentration rose to 139 mEq/liter for Na and fell to 4 mEq/liter for K. Na was absorbed at luminal concentrations above 121 mEq/liter and was secreted below this concentration. K absorption was constanty observed, but its luminal concentration was always above 4 mEq/liter. The net water flux was related to the algebraic sum of net fluxes of Na and K. The mean plasma-to-lumen fluxes of Na and K were 435 μEq/min/25 cm and 28 μEq/min/25 cm, resp., and these fluxes seemed independent of the luminal concentrations of both cations. In contrast, the lumen-to-plasma fluxes of Na and K were related to their luminal concentrations. A hyperbolic relation between lumen-to-plasma flux and luminal concentration of Na fits better with the experimental data than a linear one. In ileum, the mean plasma-to-lumen fluxes of Na and K were 288 and 25.8 μEq/min/25 cm, resp. The relations between the net movements and the luminal concentrations of Na and K did not noticeably differ in ileum, as compared with jejunum, under the conditions of this study.

6244 VITAMIN K_1 ABSORPTION BY EVERTED INTESTINAL SACS OF THE RAT. *(E.)* Hollander, D. (Albany Med. Coll., N.Y.). *Am. J. Physiol.* 225(2):360-364, 1973.

Small intestinal site and uptake mechanisms of vitamin K_1 (phylloquinone) were investigated using everted intestinal sacs in male Sprague-Dawley rats. Greater uptake of the vitamin was found in the proximal intestine compared with the distal intestine. Incubations with increasing concentrations of vitamin K_1 resulted in an apparent maximum velocity of uptake of 45 nM/100 mg sac/45 min in the proximal bowel and 14 nM/100 mg sac/45 min in the distal bowel. Incubations of the sacs under nitrogen atmosphere or at 8 C or with 2,4-dinitrophenol resulted in marked decrease of uptake by the proximal intestinal sacs but not by the distal sacs. The results suggest that vitamin K_1 uptake by the proximal small intestine is an energy-mediated process and that the proximal bowel may be the major site of absorption of vitamin K_1 in the rat.

6245 INHIBITION OF AMINO ACID TRANSPORT IN RABBIT INTESTINE BY p-CHLOROMERCURIPHENYL SULFONIC ACID. *(E.)* Schaeffer, J. F.; Preston, R. L.; Curran, P. F. (Yale Univ. Sch. Med., New Haven, Conn.). *J. Gen. Physiol.* 62(2):131-146, 1973.

Influx of phenylalanine across the brush border of rabbit intestine is reduced 80-90% by treatment with p-chloromercuriphenyl sulfonate (PCMBS, 5 mM). The effect is rapidly and completely reversed by dithiothreitol (10 mM). Phenylalanine influx into PCMBS-treated tissue can be competitively inhibited by other neutral amino acids and follows saturation kinetics. PCMBS causes an increase in the apparent Michaelis constant from the value observed in control tissue but does not alter the maximal influx significantly. Treatment of the tissue with PCMBS leads to a significant reduction in the Na-sensitivity of the transport, and a number of results indicate that the major effect of the reagent is to cause a marked reduction in the affinity of the transport system for Na. The transport system can be partially protected against reaction with PCMBS by phenylalanine (50 mM) and tryptophan (10 mM) but not by methionine or norleucine (50 mM). The transport of 3-O-methyl glucose was decreased by only 13%, suggesting that PCMBS does not cause nonspecific inhibition of all transport processes in the brush border membrane.

The results suggest that PCMBS reacts with a sulfhydryl group in the region of the transport site and may alter conformational changes associated with the binding of substrates.

6246 EFFECT OF CONJUGATED DIHYDROXY BILE SALTS ON ELECTROLYTE TRANSPORT IN RAT COLON. *(E.)* Binder, H. J.; Rawlins, C. L. (Dept. Intern. Med., Yale Univ., New Haven, Conn.). *J. Clin. Invest.* 52:1460-1466, 1973.

The effect of conjugated dihydroxy bile salts on ion transport was evaluated in the *in vitro* short-circuited colon of male Sprague-Dawley rats. Glycochenodeoxycholic acid, taurochenodeoxycholic acid, or taurodeoxycholic acid (2 mM, each) caused a prompt increase in short-circuit current and electrical potential difference. Similar results were obtained when theophylline (10 mM) was added. Removal of bicarbonate and chloride prevented the effects of both bile salts and theophylline. Pretreatment with theophylline blocked the increase in short-circuit current and potential difference produced by taurochenodeoxycholic acid and pretreatment with either taurochenodeoxycholic acid or glycochenodeoxycholic acid inhibited the expected theophylline response. Sodium fluxes in the presence of both taurochenodeoxycholic acid and theophylline demonstrated a decrease in net absorption; and taurochenodeoxycholic acid decreased net chloride absorption. Theophylline caused a reversal of net chloride absorption to net chloride secretion. It is suggested that diarrhea associated with cholerheic enteropathy is caused by active anion secretion perhaps mediated by cyclic AMP.

6247 ABSORPTION OF PROSTAGLANDINS BY THE INTESTINE AND VAGINA OF THE RAT. *(E.)* Magee, W. E.; Armour, S. B.; Miller, O. V. (Dept. Life Sci., Indiana State Univ., Terre Haute). *Biochim. Biophys. Acta* 306(2):270-282, 1973.

Because of the desirability of p.o. or topical administration of prostaglandins, an *in situ* method was used to determine the rate of absorption of prostaglandins E_2, $F_{2\alpha}$, 15-methyl $F_{2\alpha}$, and 15-methyl $F_{2\alpha}$ methyl ester from the small intestine of female Sprague-Dawley rats. Prostaglandin E_2 disappeared from the lumen with a half-life of 37 min. From 2-3% of the radioactivity was recovered in the blood at 30-60 min, but the compound was extensively metabolized, and only 0.04-0.08% of the dose was recovered intact. Absorption of the more polar prostaglandin $F_{2\alpha}$ and 15-methylprostaglandin $F_{2\alpha}$ was slower with a half-life of 60-70 min. Radioactivity in the serum at 30-60 min did not exceed 2% of the dose for animals given prostaglandin $F_{2\alpha}$ or 0.8% of the dose for animals given 15-methylprostaglandin $F_{2\alpha}$. A rapid, initial disappearance of 15-methylprostaglandin $F_{2\alpha}$ methyl ester from the small intestine was observed, followed by a second, much slower rate of absorption. The rapid phase of the absorption was extended at high dosages, resulting in blood levels of radioactivity up to 7% of the dose when 40 mg/kg were given. These results correlated with the rate of hydrolysis of the methyl ester in the lumen of the intestine, which was slower at higher doses. Little or no methyl ester was detected in serum or intestinal tissue, but up to 1.8% of the dose of intact 15-methylprostaglandin $F_{2\alpha}$ was detected in the serum at 30 min. The methyl ester of 15-methylprostaglandin $F_{2\alpha}$ was also absorbed through the large intestine and the vagina. In each case, 15-methylprostaglandin $F_{2\alpha}$ was found in the blood. Metabolites consisted of more polar acids and a component which migrated close to 15-methylprostaglandin $F_{2\alpha}$ on thin-layer chromatograms. The extent to which 15-methylprostaglandin $F_{2\alpha}$ methyl ester was metabolized by the liver was determined in a perfusion experiment. The methyl ester was hydrolyzed within 1 min, and the free acid was taken up almost quantitatively by the liver and converted into polar acids. These acids appeared in the perfusing blood and were excreted into the bile.

6248 EFFECT OF PENTAGASTRIN UPON MOVEMENTS OF WATER, ELECTROLYTES, AND GLUCOSE ACROSS THE HUMAN JEJUNUM AND ILEUM. *(E.)* Modigliani, R.; Mary, J. Y.; Bernier, J. J. (St. Lazare Hosp., Paris, France). *Digestion* 8(3):208-219, 1973.

The intestinal perfusion technique was used in 10 healthy subjects to measure the effects of pentagastrin (6 µg/kg/hr) on jejunal and ileal net and unidirectional movements from 2 isotonic solutions, 1 of which was glucose-free and the other contained 30 mM glucose. In 5 other subjects, the effect of the pentapeptide on intrajejunal transit time was assessed. In the jejunum, pentagastrin had no effect on net movements of water and electrolytes from the glucose-free solution, whereas it significantly reduced net absorption of water, sodium, potassium, and chloride from the glucose-containing solution, without affecting the absorption of glucose itself. Both jejunal unidirectional fluxes of water, sodium and potassium were reduced by pentagastrin, whatever the solution infused; but, in the presence of glucose, the insorption (lumen to blood flux) of water and electrolytes was predominantly decreased. Pentagastrin did not modify intrajejunal transit time of fluid. Ileal transport of water and ions was not affected by pentagastrin. It is suggested that pentagastrin may act through a reduction of the size of the 'pores' of the plasma membrane of the enterocyte. It is also suggested that overproduction of gastrin, as in the Zollinger-Ellison syndrome, may play a direct role in the watery diarrhea sometimes observed in this disease.

6249 EFFECT OF CHOLESTYRAMINE ON ABSORPTION OF ^{3}H DIGOXIN IN RATS. *(E.)* Thompson, W. G. (Ottawa Civic Hosp., Canada). *Am. J. Dig. Dis.* 18(10):851-856, 1973.

Intragastric ^{3}H digoxin was given to 12 rats, 6 of whom were on an 8% cholestyramine diet to determine the effect of cholestyramine on the absorption of digoxin. The cholestyramine-fed animals had a significant decrease in stool radioactivity and an increase in urine radioactivity. In another experiment 16 rats had a laparotomy and 8 of these also had common bile duct ligation. Half of each group received cholestyramine. In the sham-operated animals there was again decreased stool and increased urine recovery of radioactivity in those receiving cholestyramine. In the bile duct-tied animals, stool radioactivity decreased and urine radioactivity increased. Addition of cholestyramine to the diet did not alter the result. The apparent enhancement of digoxin absorption in intact animals by cholestyramine is explained by reduction in bile flow due to interrupted enterohepatic circulation of bile salts by the resin. This may decrease biliary excretion of digoxin.

6250 INTESTINAL ABSORPTION OF STEREOISOMERS OF DIPEPTIDES IN THE RAT. *(E.)* Asatoor, A. M.; Chadha, A.; Milne, M. D.; Prosser, D. I. (Westminster Med. Sch., London, England). *Clin. Sci. Mol. Med.* 45(2):199-212, 1973.

Jejunal absorption rates *in vivo* of the stereoisomers of alanylphenylalanine, leucyl-leucine, and glycyltryptophan were studied in male Wistar rats. Absorption rates of L-alanyl-L-phenylalanine were 200 times those of D-alanyl-D-phenylalanine; L-leucyl-L-leucine 24 times those of the DD-isomer; and glycyl-L-tryptophan 5 times those of glycyl-D-tryptophan. Mixed DL- and LD-isomers were absorbed at intermediate rates. Absorption rates were positively correlated with the rate of hydrolysis of each dipeptide by homogenates of rat intestinal mucosa. The transport rate and rate of hydrolysis of glycyl-D-tryptophan, D-alanyl-D-phenylalanine, and D-leucyl-D-leucine were significantly greater in the ileum than in the jejunum. When given by stomach tube the most slowly absorbed dipeptides, D-alanyl-D-phenylalanine, D-leucyl-D-leucine, and glycyl-D-tryptophan were the only ones excreted in significant amounts in the urine, indicating they were absorbed as the entire molecule and resistant to hydrolysis by tissue peptidases. There was a close inverse correlation between the rates of transport by rat jejunum of glycine, D-alanine, D-leucine, D-phenylalanine, D-tryptophan, D-alanyl-D-phenylalanine, D-leucyl-D-leucine, and glycyl-D-tryptophan and the molecular weight of each compound. This suggests that diffusion mechanisms are important in jejunal absorption of these compounds. No such correlation was found in the case of the ileum.

6251 THE EFFECTS OF TRIGLYCERIDE ABSORPTION UPON GLUCAGON, INSULIN, AND GUT GLUCAGON-LIKE IMMUNOREACTIVITY. *(E.)* Bottger, I.; Dobbs, R.; Faloona, G. R.; Unger, R. H. (Dept. Internal Med., Univ. Texas, Dallas). *J. Clin. Invest.* 52(10):2532-2541, 1973.

The effects of a fat meal upon plasma insulin, glucagon, and glucagon-like immunoreactivity were studied in conscious dogs and human volunteers. The intraduodenal instillation of 10 g/kg of peanut oil was accompanied in dogs by increases in the mean plasma levels of all 3 polypeptides that averaged 5 µU/ml, 107 pg/ml, and 2.1 ng/ml, resp. When emulsified with egg yolk, 3 g/kg of peanut oil elicited a much greater response of the 3 hormones. A physiologic dose of 1 g/kg in emulsified form also caused a significant rise in glucagon and glucagon-like immunoreactivity. The islet cell hormone response was not due to chylomicronemia, for i.v. infusion of canine chyle did not stimulate glucagon secretion. Moreover, in dogs with a thoracid duct fistula in which chyle was excluded from the circulation, the intraduodenal administration of a fat meal elicited the normal islet cell hormone response, as well as a rise in glucagon-like immunoreactivity. Medium-chain triglycerides (10 g/kg) did not elicit these responses. In 6 human volunteers the administration of peanut oil (3 g/kg, p.o.) was accompanied by increments of 2 µU/ml, 26 pg/ml, and 1.5 ng/ml in the mean levels of insulin, glucagon, and glucagon-like immunoreactivity, resp. The changes in insulin and glucagon in man were neither statistically significant nor biologically impressive. It is concluded that fat absorption in dogs is accompanied by prompt and substantial increases in plasma glucagon and glucagon-like immunoreactivity and a small transient rise in insulin. The evidence favors an enterogenic signal, e.g. pancreozymin, to the islets of Langerhans rather than their stimulation by chylomicrons.

6252 EMBRYONIC CHICK INTESTINE IN ORGAN CULTURE. A UNIQUE SYSTEM FOR THE STUDY OF THE INTESTINAL CALCIUM ABSORPTIVE MECHANISM. *(E.)* Corradino, R. A. (New York State Vet. Coll., Ithaca). *J. Cell. Biol.* 58(1):64-78, 1973.

Excellent preservation of mucosal structure at both the light and electron microscope levels was obtained in duodena from 20-day-old chick embryos in large-scale organ culture on specially designed stainless-steel grids in contact with serum-free medium for 48 hr. Although mitotic rate was subnormal, several other factors attest to the essential viability of the cultured intestine: L-leucine incorporation into protein, as well as the synthesis of a specific vitamin D_3 induced calcium-binding protein, increased over a 48-hr culture period, and the electropotential gradient across the intestine was maintained throughout the culture period as was a concentration gradient for calcium. The tissue responded to vitamin D_3 in the medium by synthesizing the calcium-binding protein within 6 hr and by exhibiting enhanced ^{45}Ca uptake within 12-24 hr. Concentrations of vitamin D_3, or its 25-hydroxylated derivative, higher than necessary for calcium-binding protein induction, also increased the activity of alkaline phosphatase. The 1,25-dihydroxylated derivative of vitamin D_3, at a level extremely potent in calcium-binding protein induction, did not stimulate alkaline phosphatase. Mucosal-to-serosal transport of ^{45}Ca could also be measured in everted duodenal sacs, subsequent to culture under similar conditions, and was also increased by vitamin D_3 in the medium. Other embryonic organs, esophagus, stomach, liver, pancreas, lung, skin, and muscle, did not produce calcium-binding protein in response to vitamin D_3 in the culture medium. However, calcium-binding protein synthesizing capacity was present in the entire intestinal tract, except in the rectum. ^{59}Fe and ^{32}P uptake by cultured duodenum were also stimulated by vitamin D_3. This system is useful in the study of the vitamin D-mediated calcium absorptive mechanism but should be applicable to the study of the absorption of other nutrients, drugs, and hormones, as well as other studies of intestinal function.

6253 ROLE OF INTESTINAL ALKALINE PHOSPHATASE IN FAT TRANSPORT. *(E.)* Lam, K. C.; Mistilis, S. P. (Roy. Prince Alfred Hosp., Camperdown, Australia). *Aust. J. Exp. Biol. Med. Sci.* 51(3):411-416, 1973.

Digestion, absorption, and intestinal transport of intraduodenally infused lipids were studied sequentially in male Sprague-Dawley rats to define the mechanism responsible for the marked increase in intestinal alkaline phosphatase in lymph following fat ingestion. The increase in lymph intestinal alkaline phosphatase observed after infusion of lipids and fatty acids of various chain lengths was not related to intraluminal fat digestion or to transport of long- or short-chain fatty acids across mucosal brush borders, and was not a structural part of lipoprotein particles in lymph. The increase was related to triglyceride or lipoprotein synthesis in the endocytoplasmic reticulum, or closely involved with the transport of lipoprotein through the cell and its passage across plasma membranes into the interstitial space by reverse pinocytosis. It is suggested that the endoplasmic reticulum appearing in lymph may be the vesicle membrane observed in intestinal cells following fat ingestion and that alkaline phosphatase is part of this membrane which dissociates from the lipid droplets during reverse pinocytosis.

6254 EFFECTS OF SMALL-INTESTINAL FUNCTION AND STRUCTURE INDUCED BY FEEDING A DECONJUGATED BILE SALT. *(E.)* Gracey, M.; Papadimitriou, J.; Burke, V.; Thomas, J.; Bower, G. (Princess Margaret Children's Med. Res. Fdn., Perth, Australia). *Gut* 14(7):519-528, 1973.

Feeding sodium deoxycholate orally to adult Wistar rats for 3 days inhibited small-intestinal active sugar transport and ouabain-sensitive, sodium-potassium-dependent adenosine triphosphatase activity. There was also evidence of extensive ultrastructural damage to the microvillar and intracellular compartments of the small-intestinal epithelium while its light microscopic appearance was essentially normal. These functional and morphological changes reverted toward normal over the subsequent 4 days when a normal diet, without added bile salt, was reintroduced. This method of studying the relation of bile salts to intestinal sugar transport may be more relevant than acute experiments to clinical situations in which deconjugated bile salts affect small intestinal functions over days, weeks, or months, rather than for minutes or a couple of hours as in acute experiments.

6255 INTESTINAL VITAMIN B_{12} ABSORPTION AND GASTRIC JUICE IN THE CAT. *(E.)* Okuda, K.; Kitazaki, T.; Morokuma, M. (Chiba Univ. Sch. Med., Japan). *Am. J. Dig. Dis.* 8(5):417-428, 1973.

Intestinal absorption of ^{57}Co-B_{12} (cyanocobalamin) was studied in the cat. Doses of B_{12} (5-1000 ng, p.o.) were absorbed with little difference percentagewise. When these doses were placed in the ileal sacs prepared *in vivo*, the percent absorption was greater in large than in small doses. Addition of homologous gastric juice inhibited absorption. Pancreatic juice given with the small dose increased its absorption. Cat gastric juice and a saline extract of gastric mucosa contained vitamin B_{12} binding proteins as demonstrated by Sephadex G-200 filtration and DEAE-cellulose chromatography after dialysis with a tracer amount of ^{57}Co-B_{12}. Therefore, the cat lacks gastric intrinsic factor that aids absorption of small doses of vitamin B_{12} from the ileum. It is suggested, however, that in cats the role of vitamin B_{12} binding proteins in gastric juice differs from the role of intrinsic factor in man.

6256 COUPLED SODIUM-CHLORIDE INFLUX ACROSS THE BRUSH BORDER OF RABBIT ILEUM. *(E.)* Nellans, H. N.; Frizzell, R. A.; Schultz, S. G. (Univ. Pittsburgh Sch. Med., Pa.). *Am. J. Physiol.* 225(2):467-475, 1973.

About 20% of the total sodium and chloride influxes across the brush border of rabbit ileum are mediated by an obligatory one-for-one coupled sodium chloride influx process that is inhibited by theophylline (10 mM, incubation 20 min prior to influx determination). Theophylline does not inhibit sodium influx in the absence of sodium, suggesting that its effect is restricted to this coupled process. Kinetic analyses indicate that reducing the concentration of sodium and/or chloride in the mucosal solution reduces the maximal influx of the coupled process and simulates the effects of theophylline which behaves as a strict noncompetitive inhibitor of this mechanism. The kinetic data suggest that the random combination of sodium and chloride with a membrane component forms a ternary complex with the restriction that only the free (unloaded) "carrier" and the ternary complex are capable of translocation across the mucosal membrane. These observations provide an explanation for the simultaneous reductions in the unidirectional mucosa-to-serosa fluxes of sodium and chloride across rabbit ileum elicited by theophylline, cyclic AMP, and cholera toxin. Inhibition of this coupled sodium chloride influx process at the mucosal membrane may be significant in the pathogenesis of clinical cholera.

6257 EFFECT OF K^+ AND K^+ GRADIENTS ON ACCUMULATION OF SUGARS BY ISOLATED INTESTINAL EPITHELIAL CELLS.

(E.) Kimmich, G. A.; Randles, J. (Univ. Rochester Sch. Med. Dent., N.Y.). *J. Membrane Biol.* 12:23-46, 1973.

With the use of isolated intestinal epithelial cells, the role of transmembrane K^+ gradients in providing an energy input for Na^+-dependent monosaccharide transport systems was evaluated. Experimentally imposing a K^+ gradient in a sense reversed from normal did not lead to extrusion of sugar from cells pre-equilibrated with ^{14}C-3-O-methylglucose, even in situations were a reversed Na^+ gradient was also imposed. Furthermore, cells preloaded with K^+ showed no better ability to accumulate 3-O-methylglucose that K^+-depleted cells, when the 2 populations were compared under identical incubation conditions. Fluxes of K^+ associated with the sugar carrier could not be detected in terms of suspected sensitivity to agents which immobilize the sugar carrier. In addition, fluxes of sugar in response to imposed K^+ gradients were not demonstrable in cells de-energized by preincubation with dinonyl phthalate, no matter in which direction the K^+ gradient was imposed. Finally, the severe inhibitory effects of K^+ on Na^+-dependent sugar transport by the cells disappeared in de-energized cells, despite the fact that Na^+-dependent carrier-mediated sugar entry still occurred. These facts are difficult to reconcile with a significant role for cellular K^+ gradients in supporting active sugar transport as envisioned by the ion gradient hypothesis. Instead, a fundamental Na^+-dependent energy transductive event is suggested which depends on ATP, and which can generate a membrane-bound energized intermediate that serves to support a variety of active transport events. An analogy is drawn between this concept for animal cell plasma membranes and the better documented phosphotransferase system for sugar transport described for certain microorganisms.

6258 INCORPORATION OF ^{32}P AND ^{3}H-LABELED FATTY ACIDS IN PHOSPHOLIPIDS OF THE INTESTINAL MUCOSA.

(Fr.) Di Costanzo, G.; Mathieu, D.; Pecquery, R. (Lab. Metabolic Physiol. Nutrition, Univ. Paris, France). *Biochimie* 55(2):213-220, 1973.

Incorporation of ^{32}P-labeled sodium phosphate into phospholipids was studied in the first 1/3 of the intestine in fasted and nonfasted adult Wistar rats 15 min to 24 hr after i.p. injection of ^{32}P. The intestine was extracted with chloroform:methanol (4:1) and the extract chromatographed on columns of silica and Supercel by elution with mixtures of chloroform and methanol. The rate of incorporation of ^{32}P was relatively slow and was the same for all phospholipid constituents in the intestine of fasted rats; incorporation of ^{32}P reached a maximum about 8 hr after injection of ^{32}P. In addition to this slow turnover, a rapid turnover was observed in nonfasted rats for all phospholipids with the exception of phosphatidylethanolamines and phosphatidylserines. After a 17-hr fast, rats were fed a synthetic fat-free diet to which 400 mg lipids had been added. Lipids contained 40 mg of fatty acids labeled with ^{3}H on carbons 9 and 10. ^{3}H-labeled oleic acid was added to a mixture of sunflower seed oil and lanolin, and ^{3}H-labeled palmitic acid was added to olive oil. Rats were sacrificed 30 min to 6 hr after feeding. The incorporation of both fatty acids into phosphatidylethanolamines and phosphatidylserines increased progressively with time, but the incorporation of palmitic acid occurred sooner than that of oleic acid. Phosphatidylinositols incorporated little of either fatty acid, while sphingomyelins incorporated little oleic acid but incorporated palmitic acid 2-3 hr after ingestion. ^{3}H-labeled fatty acids were incorporated into polyglycerophosphatides + phosphatidic acids within the first 3 hr. Maximum incorporation of fatty acids into phosphatidylcholines occurred at 1 and 3-4 hr. These findings indicate that phosphatidic acids + polyglycerophosphatides are involved with the transport of fatty acids, while phosphatidylcholines take part in their synthesis. Phosphatidylinositols are involved with fatty acid absorption and the transport of molecules other than lipids.

6259 REGIONAL INTESTINAL ABSORPTIVE CAPACITIES FOR TRIOLEIN: AN ALTERNATIVE TO MARKERS.

(E.) Clark, S. B.; Lawergren, B.; Martin, J. V. (St. Luke's Hosp. Ctr., New York, N.Y.). *Am. J. Physiol.* 225(3):574-585, 1973.

The absorption and transport of 1-^{14}C-triolein by different regions of unresected rat small intestine were evaluated in unanesthetized male Wistar rats. Luminal lipolysis was regulated by absorption rate during maximal-rate infusion. Absorption was maximal within the 1st hr and remained constant for at least 4 hr. In the proximal intestinal wall the lipid concentration reached a steady state within 1 hr, whereas distally fat continued to accumulate. In all regions ^{14}C-labeled tissue lipid was predominantly triglyceride. Thus the capacity of the distal intestine to release chylomicron lipid may be limited. Marker methods traditionally used to determine fat absorption are questionable in small animals *in vivo* because of the unequal propulsion of different components of the meal. A mathematical model describing maximal uptake and transmucosal transport in all regions of small intestine was prepared. Uptake rate/unit intestinal weight was constant in the first 70% of the intestine and slowed thereafter, while lipid output rates on the serosal side slowed progressively from duodenum and leveled off in the terminal 30% of intestine. A method was also introduced which allows fatty acid turnover rates through mucosal lipid compartments to be compared in a single tissue analysis in tissues that are in a steady state.

6260 ADAPTIVE UPTAKE OF CALCIUM AT THE DUODENAL BRUSH BORDER. *(E.)* Walling, M. W.; Rothman, S. S. (Harvard Med. Sch., Boston, Mass.). *Am. J. Physiol.* 225(3):618-623, 1973.

Initial rates of calcium uptake at the brush border of the duodenum in growing male Holtzman rats were measured *in vitro*. A constant rate of uptake was found for 60-80 sec. Inhibition of aerobic metabolism increased the initial uptake rate, but decreased calcium uptake over a 6-min period. Dietary calcium deprivation produced equivalent increases in initial rates and 3-min uptake measurements at low-calcium concentrations. However, at 10 mM calcium, the 3-min uptake rate became saturated in calcium-deprived rats, whereas initial rates from both normal and calcium-deprived rats and normal 3-min uptake values increased in proportion to changes in calcium concentration. The active transport step in calcium absorption is apparently internal to the process measured as initial uptake, since saturation kinetics are not observed for initial rates over a range of calcium concentrations where mucosal-to-serosal flux saturates and because longer uptake intervals are required to demonstrate both metabolic inhibition and saturation kinetics. The increased initial uptake rates that result from dietary calcium restriction indicate that at least part of the transport adaptation which produces increased calcium absorption involves changes in uptake or binding by the brush border.

6261 ABSORPTION OF IRON FROM SUSTAINED RELEASE AND RAPIDLY DISINTEGRATING TABLETS. INFLUENCE OF DAILY NUMBERS OF ADMINISTRATIONS. *(E.)* Nielsen, J. B.; Ikkala, E.; Sclvell, L.; Bjorn-Rasmussen, E.; Ekenved, G. (Rigshosp., Copenhagen, Denmark). *Acta Med. Scand.* 194(1/2):123-127, 1973.

6262 ROLE OF UPTAKE PHENOMENA IN THE SENSITIZING EFFECT OF METABOLIC INHIBITORS ON RESPONSE OF ISOLATED RAT INTESTINE TO THE ACTION OF SYMPATHOMIMETIC AGENTS. *(Fr.)* Valette, G.; Leclair, M. F. (Fac. Pharm., Paris, France). *Biochem. Pharmacol.* 21:1861-1869, 1972.

6263 EFFECT OF COLESTIPOL ON GASTROINTESTINAL ABSORPTION OF CHLOROTHIAZIDE IN MAN. *(E.)* Kauffman, R. E.; Azarnoff, D. L. (Univ. Kansas Med. Ctr., Kansas City). *Clin. Pharmacol. Ther.* 14(5): 886-890, 1973.

6264 ASBESTOS FIBERS IN BEVERAGES, DRINKING WATER, AND TISSUES: THEIR PASSAGE THROUGH THE INTESTINAL WALL AND MOVEMENT THROUGH THE BODY. *(E.)* Cunningham, H. M.; Pontefract, R. D. (Food Res. Lab., Health Protection Br., Ottawa, Canada). *J. Assoc. Off. Anal. Chem.* 56(4):976-981, 1973.

6265 THE INFLUENCE OF METOCLOPRAMIDE ON DRUG ABSORPTION. *(E.)* Nimmo, J. (Roy. Infirm., London, England). *Postgrad. Med. J.* 49(4):25-28, 1973.

6266 MORPHOLOGY AND FUNCTION IN JEJUNAL BYPASSED SMALL INTESTINE AFTER RECONSTITUTION. *(Ger.)* Menge, H.; Bloch, R.; Lorenz Meyer, H.; Riecken, E. O. (Med. Clin., Univ. Marburg/Lahn, Germany). *Res. Exp. Med.* 161(2):133-140, 1973.

6267 THIRST SATIATION AND THE TEMPERATURE OF INGESTED WATER. *(E.)* Deaux, E. (Dept. Psychol., Antioch Coll., Yellow Springs, Ohio). *Science* 181(4105):1166-1167, 1973.

6268 TECHNIQUES FOR INTESTINAL PERFUSION IN MAN. *(Fr.)* Rousseau, B. (Notre Dame Hosp., Montreal, Canada). *Union Med. Can.* 102(1): 140-144, 1973.

6269 COMPARATIVE METABOLISM OF LEAD AND CALCIUM IN YOUNG AND ADULT RATS. *(E.)* Kostial, K.; Kello, D.; Harrison, G. H. (Inst. Med. Res., Zabreb, Yugoslavia). *Int. Arch. Arbeitsmed.* 31(2):159-161, 1973.

6270 INDICES OF VIABILITY OF ISOLATED INTESTINES: GLUCOSE UPTAKE AND RELEASE OF ENZYMES. *(E.)* Kimura, S.; Totani, M.; Murachi, T. (Nagoya City Univ. Sch. Med., Japan). *Jap. J. Exp. Med.* 43(3): 163-177, 1973.

6271 RECTAL ABSORPTION OF ^{99m}Tc-PERTECHNETATE IN THE DOG. *(E.)* Caride, V. J. (Yale Univ. Sch. Med., New Haven, Conn.). *J. Nucl. Med.* 14(8):600-603, 1973.

6272 EFFECT OF CHELATING AGENTS ON CHROMIUM ABSORPTION IN RATS. *(E.)* Chen, N. S. C.; Tsai, A.; Dyer, I. A. (Anim. Sci. Dept., Washington State Univ., Pullman). *J. Nutr.* 103(8):1182-1186, 1973.

6273 EFFECT OF BILE SALTS ON PARTITIONING BEHAVIOR AND GI ABSORPTION OF A QUATERNARY AMMONIUM COMPOUND, ISOPROPAMIDE IODIDE. *(E.)* Gaginella, T. S.; Bass, P.; Perrin, J. H.; Vallner,

J. J. (Sch. Pharm., Univ. Wisconsin, Madison). *J. Pharm. Sci.* 62(7):1121-1125, 1973.

6274 BIOCHEMICAL, MORPHOLOGICAL AND FUNCTIONAL INVESTIGATIONS ON THE EFFECT OF PHENFORMIN ON SMALL INTESTINAL MUCOSA IN RAT AND IN MAN. *(Ger.)* Bloch, R.; Menge, H.; Schaarschmidt, W. D.; Gottesburen, H.; Schaumloffel, E.; Goebell, H.; Riecken, E. O. (Med. Clin., Univ. Murburg, Germany). *Klin. Wochenschr.* 51(5):235-241, 1973.

6275 EFFECT OF 2-AMINOETHANESULPHONIC ACID (TAURINE) AND 2-HYDROXYETHANE SULPHONIC ACID (ISETHIONIC ACID) ON CALCIUM TRANSPORT BY RAT LIVER MITOCHONDRIA. *(E.)* Dolara, P.; Marino, P.; Buffoni, F. (Dept. Pharmacol., Univ. Florence, Italy). *Biochem. Pharmacol.* 22(17):2085-2094, 1973.

6276 PURINE NUCLEOTIDE BIOSYNTHESIS IN GASTROINTESTINAL MUCOSA. *(E.)* Mackinnon, A. M.; Deller, D. J. (Dept. Med., Univ. Adelaide, Australia). *Biochim. Biophys. Acta* 319(1):1-4, 1973.

6277 RADIOAUTOGRAPHIC OBSERVATIONS ON IRON ABSORPTION BY THE DUODENUM OF MICE WITH IRON OVERLOAD, IRON DEFICIENCY, AND X-LINKED ANEMIA. *(E.)* Bedard, Y. C.; Pinkerton, P. H.; Simon, G. T. (Sunnybrook Hosp., Toronto, Canada). *Blood* 42(1):131-140, 1973.

6278 RETENTION OF A SINGLE ORAL MASSIVE DOSE OF VITAMIN A. *(E.)* Pereira, S. M.; Begum, A. (Christian Med. Coll., Tamil Nadu, India). *Clin. Sci. Mol. Med.* 45(2):233-237, 1973.

6279 VITAMIN D AND INTESTINAL TRANSPORT OF CALCIUM: EFFECTS OF PREDNISOLONE. *(E.)* Lukert, B. P.; Stanbury, S. W.; Mawer, E. B. (Univ. Kansas Med. Ctr., Kansas City). *Endocrinology* 93 (3):718-722, 1973.

6280 GASTROINTESTINAL ABSORPTION OF DIFFERENT COMPOUNDS OF ^{115}mCADMIUM AND THE EFFECT OF DIFFERENT CONCENTRATIONS IN THE RAT. *(E.)* Moore, Jr., W.; Stara, J. F.; Crocker, W. C. (Environ. Toxicol. Res. Div., Environ. Prot. Agency, Cincinnati, Ohio). *Environ. Res.* 6(2):159-164, 1973.

6281 BILIARY EXCRETION BEHAVIOR DIFFERENCE OF QUATERNARY AMMONIUM COMPOUNDS BETWEN PORTAL VEIN AND FEMORAL VEIN INFUSION IN RAT. *(E.)* Oguma, T.; Muramatsu, T.; Iga, T.; Fuwa, T.; Awazu, S.; Hanano, M. (Fac. Pharm. Sci., Univ. Tokyo, Japan). *Chem. Pharm. Bull.* 21(7):1554-1559, 1973.

6282 ABSORPTION OF VITAMIN B_{12} IN RELATION TO PROPULSIVE INTESTINAL MOTILITY IN THE RAT. *(E.)* Gronqvist, B. (Univ. Hosp., Uppsala, Sweden). *Acta Chir. Scand.* 139(4):384-391, 1973.

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6284 THE RELATIONSHIP OF INTRACELLULAR PATHWAYS OF IRON METABOLISM TO CELLULAR IRON OVERLOAD AND THE IRON STORAGE DISEASES. *(E.)* Trump, B. F.; Valigorsky, J. M.; Arstila, A. U.; Mergner, W. J.; Kinney, T. D. (Duke Univ. Med. Ctr., Durham, N.C.). *Am. J. Pathol.* 72(2):295-324, 1973.

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6288 THE EFFECT OF GASTRIC SECRETIONS ON IRON ATTACHMENT TO THE SMALL INTESTINE. *(E.)* Kimber, C. L.; Mukherjee, T. (Ist. Med. Vet. Sci., Adelaide, Australia). *Pathology* 5(1):31-38, 1973.

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6304 ABSORPTION, DISTRIBUTION AND EXCRETION OF K-STROPHANTHOSIDE (^{3}H) ADMINISTERED RECTALLY TO GUINEA-PIGS. *(E.)* Marzo, A.; Ghirardi, P.; Croce, G.; Marchetti, G. (Simes Inst. Exptl. Cardiol.-Biochem., Milan, Italy). *Naunyn Schmiedebergs Arch. Pharmakol.* 279(1):19-29, 1973.

6305 UTILIZATION OF NUTRIENTS IN MILK- AND WHEAT-BASED DIETS BY MEN WITH ADEQUATE AND REDUCED ABILITIES TO ABSORB LACTOSE. I. ENERGY AND NITROGEN. *(E.)* Calloway, D. H.; Chenoweth, W. L. (Dept. Nutr. Sci., Univ. California, Berkeley). *Am. J. Clin. Nutr.* 26(9):939-951, 1973.

6306 INTESTINAL ABSORPTION OF ^{45}CA AND ^{89}Sr AS AFFECTED BY Ca, Sr, AND Mg. *(E.)* Mraz, F. R. (Agr. Res. Lab., Univ. Tennessee, Oak Ridge). *Poult. Sci.* 52(3):1208-1209, 1973.

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6309 EFFECT OF CHOLINERGIC DRUGS ON CALCIUM MOVEMENT IN GUINEA PIG.TAENIA COLI. *(E.)* Nasu, T.; Urakawa, N. (Dept. Vet. Pharmacol., Univ. Tokyo, Japan). *Jap. J. Pharmacol.* 23(4):553-561, 1973.

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OF SUGARS ON CALCIUM ABSORPTION. *(Fr.)* Fournier, P.; Digaud, A.; Dupuis, Y.; Fournier, A. (Practical Sch. Higher Education, Paris, France). *C. R. Acad. Sci. (Paris)* 276(10):1581-1584, 1973.

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6313 EFFECT OF DIETARY FAT SATURATION ON ABSORPTION AND INTESTINAL SECRETION OF CHOLESTEROL BY THE HYPERCHOLESTEROLEMIC RAT. *(E.)* McGovern, R. F.; Quackenbush, F. W. (Dept. Biochem., Purdue Univ., West Lafayette, Ind.). *Lipids* 8(8):470-472, 1973.

See also, 6140, 6203, 6231, 6360, 6622, 7340, 7489, 7590, 8020.

MOTILITY

6314 THE EFFECT OF DISTAL AND ISOPERISTALTIC TRANSPLANTATION OF A JEJUNAL SEGMENT ON INTESTINAL MOTILITY AND EVACUATION. *(Fr.)* Eyskens, E.; Peeters, T.; Hellemans, J.; Vantrappen, G. (Lab. Exp. Surg., Catholic Univ., Louvain, Belgium). *Acta Gastroenterol. Belg.* 36(1/2):105-125, 1973.

An isoperistaltic segment of proximal jejunum, 20 cm long, was transplanted to the terminal ileum in 56 dogs. Changes in motor activity were studied by electromanometry and electromyography, and $^{51}Cr_2O_3$ was employed as a marker to study changes in transit time. Controls consisted of 26 dogs with intact small intestines and 20 dogs with 3 intestinal anastomoses without jejunal transplantation. At 5-7 days after surgery, the basal electrical rhythm was decreased and the configuration of electrical complexes in the transplanted jejunum resembled those of ileal complexes. Thereafter, a progressive increase occurred in the basal electrical rhythm and electrical complexes acquired a typical jejunal configuration. The gradient in intestinal motor activity was decreased from 14% to 9% by jejunal transplantation. After recent surgery, spontaneous activity in the transplanted jejunum was the same as that in the adjacent ileum but significantly lower than that in the intact jejunum, even after electrical stimulation of the transplanted jejunum. At 2 months or more after jejunal transplantation, spontaneous intestinal activity was the same as in dogs with intact small intestines. After stimulation, the transplanted jejunum was more active than either the ileum or intact jejunum. Intestinal transit time was significantly longer in dogs who had undergone jejunal transplantation 2 months or more previously than it was in the other 2 groups. However, the mean increase in transit time (about 1 hr) is not great enough to justify the use of this operation for therapeutic purposes. This study does, however, reinforce the conclusion that the control of intestinal evacuation is dependent upon a pressure gradient.

6315 THE EFFECT OF CAERULEIN ON THE LOWER OESOPHAGEAL SPHINCTER IN MAN AND DOG. *(E.)* Jennewein, H. M.; Siewert, R.; Waldeck, F. (C. H. Boehringer Sohn, Ingelheim/Rhine, Germany). *Germ. Med.* 3(1):8-9, 1973.

Because the action of caerulein on the smooth musculature of the gastrointestinal tract differs markedly according to the site, experiments were conducted to determine its effect on the lower esophageal sphincter in man and dog. Maximal pressure in the lower esophageal sphincter, as measured by a continuous withdrawal method with a perfused catheter, was used as the indicator for sphincter tone. Individual measurements were made in the dog at intervals of one min and in healthy human subjects at intervals of 5 min. Single injections of caerulein (20 ng/kg i.v.) in man caused an average fall (6 trials) in the maximal sphincter pressure from 19 ± 1.3 mm Hg to 11 ± 1.8 mm Hg. Corresponding results were obtained in the dog after single injections. Continuous infusion of caerulein (200 ng/kg/hr) in the dog caused no change in the resting pressure of the sphincter, apart from an initial but transitory increase. Analysis of data indicated that caerulein, similar to gastrin, has a stimulating effect on the lower esophageal sphincter; this effect is definitely weaker than that of gastrin. The maximal change in sphincter pressure is quantitively reduced by caerulein infusion. Related experiments are being undertaken to further elucidate these relationships.

6316 NERVE-MEDIATED INHIBITION OF MECHANICAL ACTIVITY IN RABBIT DUODENUM AND THE EFFECTS OF DESENSITIZATION TO ADENOSINE AND SEVERAL OF ITS DERIVATIVES. *(E.)* Weston, A. H. (Dept. Pharmacol., Univ. Manchester, England). *Br. J. Pharmacol.* 48(2):302-308, 1973.

Inhibition of mechanical activity in longitudinal muscle strips of rabbit duodenum was induced by perivascular and intramural nerve stimulation. The effects of perivascular stimulation were abolished by phentolamine (2.5 μM) + propranolol, (4.75 μM) guanethidine (10 μM), reserpine, and tetrodotoxin. The effects of intramural stimulation were abolished only by tetrodotoxin (313 nM). Noradrenaline, phenylephrine, isoprenaline, ATP, ADP, AMP (0.16-40 μM), and adenosine (0.16-40 μM) each produced an inhibition of mechanical activity. The relative potencies of these agonists were noradrenaline > isoprenaline > phenylephrine > ATP > ADP > adenosine > AMP. Exposure of tissues to high concentrations of either ATP or adenosine desensitized the tissue to further exposure to ATP, ADP, AMP, and adenosine. The inhibitory effects of noradrenaline, phenylephrine, and isoprenaline and of perivascular and intramural stimulation were unaffected. The effects of desensitization were reversible. It was concluded that the effects of intramural stimulation were mediated neither by noradrenaline nor by adenosine or its derivatives.

6317 ANALYSIS OF THE PERISTALTIC REFLEX IN VITRO: EFFECTS OF SOME ANTAGONISTS. *(E.)* Fontaine, J.; Van Nueten, J. M.; Janssen, P. A. (Lab. Pharmacodyn. Ther., Free Univ. Brussels, Belgium). *Arch. Int. Pharmacodyn. Ther.* 203(2):396-399, 1973.

The effects of atropine sulfate, hexamethonium bromide, procaine chlorhydrate, and tetrodotoxin on the peristaltic reflex of isolated guinea-pig ileum were studied. Total inhibition of each parameter of reflex activity was observed only with tetrodotoxin, an 0.010 mg/liter dose completely inhibiting circular muscle activity and fluid expulsion and an 0.63 dose totally inhibiting longitudinal muscle response. Hexamethonium and procaine (10 mg/liter) were able to inhibit completely circular muscle activity and fluid explosion with only partial inhibition of the longitudinal muscle activity. Even at high doses (0.16 mg/liter), atropine was unable to inhibit the nongraded part of longitudinal activity or to block the circular activity and related fluid expulsion. The inhibitory effects observed appeared to be reversible for the 4 compounds. The data suggest that one or several cholinergic synapses are involved in the circular reflex and its propagation. In the longitudinal reflex the responses are only partially cholinergic and the involvement of a noncholinergic synpase, or even the absence of synpase, must be assumed. An important part is due to a noncholinergic transmitter of unknown nature. Relaxation of the longitudinal muscle appears to be an active process and neuromuscular transmission is mainly cholinergic.

6318 VAGO-VAGAL GASTRO-GASTRIC RELAXATION IN THE CAT. *(E.)* Abrahamsson, H.; Jansson, G. (Dept. Physiol., Univ. Goteborg, Sweden). *Acta Physiol. Scand.* 88(3):289-295, 1973.

Electric afferent stimulation of nerve branches emanating from the gastric corpus region in 17 anesthetized cats promptly elicited reflex gastric relaxation. The response was not blocked by atropine (0.5-1.0 mg/kg, i.v.), guanethidine (3-4 mg/kg), or cervical spinal cord transection but was abolished by cervical vagotomy, showing that the vagal "relaxatory" fibers to the stomach mediate this reflex ef effect. Transient distension of the stomach produced long-lasting gastric relaxation with similar characteristics to that obtained by the afferent electric stimulation. It was by vagal blockade experiments in atropinized cats that the vagal nerves exert no or only slight relaxatory effects if the stomach is only slightly filled, but have a profound relaxatory effect when the stomach is moderately or greatly filled. It is concluded that a vago-vagal gastrogastric relaxatory reflex exists where the vagal nonadrenergic relaxatory fibers serve as the efferent link. The reflex can be activated from gastric mechanoreceptors responding to distension and is suggested to be involved in the regulation or receptive relaxation in gastric filling.

6319 VAGAL RELAXATION OF THE STOMACH INDUCED BY APOMORPHINE IN THE CAT. *(E.)* Abrahamsson, H.; Jansson, G.; Martinson, J. (Dept. Physiol., Univ. Goteborg, Sweden). *Acta Physiol. Scand.* 88(3):296-302, 1973.

In anesthetized or decrebrate unanesthesized cats administration of the emetic drug apomorphine (0.2-30 mg/kg as i.v. infusion or 0.1-30 mg/kg directly into the right vertebral artery) produced pronounced and long-lasting relaxation of the stomach. When apomorphine induced somatomotor retching or vomiting movements these were always preceded by gastric relaxation. The gastric relaxatory response to apomorphine could not be blocked by atropine (0.5-0.8 mg/kg, i.v.) or guanethidine (3.5 mg/kg, i.v.) but was completely abolished after vagotomy. Vagotomy, if performed during the relaxed state of the stomach after apomorphine administration, resulted in a prompt decrease of gastric volume. Injection of apomorphine had no essential effect on gastric contractions induced by efferent electrical vagal stimulation, indicating that the splanchne nerves were of minor or no importance for the apomorphine-induced gastric relaxation. It is concluded that apomorphine produces gastric relaxation by activation of the vagal nonadrenergic relaxatory nerve fibres to the stomach. The results indicate that the relaxation of the proximal part of the stomach known to appear early in the vomiting act, is mediated by these relaxatory nerve fibers.

6320 THE EFFECTS OF VARYING THE EXTENT OF THE VAGOTOMY ON THE MYOELECTRICAL AND MOTOR ACTIVITY OF THE STOMACH. *(E.)* Stoddard, C. J.; Waterfall, W. E.; Brown, B. H.; Duthie, H. L. (Sheffield Roy. Infirm., England). *Gut* 14(8): 657-664, 1973.

The effects of varying the extent of vagotomy on the myoelectrical and motor activity of the stomach were studied in 21 patients undergoing truncal, selective, or highly selective vagotomy for the treatment of chronic duodenal ulceration. The mean percentage time that regular antral myoelectrical activity was recorded preoperatively was 95.8% and this was decreased following highly selective vagotomy (74.0%), selective vagotomy (37.8%), and truncal vagotomy (30.2%). The mean amplitude of the pacesetter potential was less following truncal (0.86 mV), selective (1.32 mV) and highly selective vagotomy (1.67) than in preoperative studies (2.21 mV). Following truncal and selective vagotomies the triphasic waveform of the pacesetter potential changed to a sinusoidal shape. No significant change in the mean preoperative frequency of the myoelectrical activity (3.03 cpm) occurred after vagotomy. Thus, the changes in the electrical activity of the stomach are related to the extent of the vagal denervation, particularly to an alteration in the balance between the vagal and sympathetic nervous supply to the stomach. Preservation of the vagal nerves to the antrum will ensure its normal motor function. Administration of insulin i.v. did not alter the electrical patterns except after highly selective vagotomy when the amplitude of the electrical waves, the incidence of action potentials, and percentage motor activity were increased.

6321 PROPULSIVE MOTILITY AFTER TRANSPOSITION OF THE JEJUNUM AND ILEUM IN THE RAT. *(E.)* Gronqvist, B. (Univ. Hosp., Uppsala, Sweden). *Acta Chir. Scand.* 139(4):377-383, 1973.

The propulsive motility of the small intestine was investigated in 64 male Sprague-Dawley rats after transposition of the jejunum and ileum in which the positions of the proximal and distal halves of the small intestine were interchanged. Weight gain in the transposed animals was slightly less than in controls. When tested up to 12 weeks postoperatively, the transposed segments of small intestine had not adapted to their new positions; the distal part retained its slow propulsive motility and, although more difficult to evaluate, the proximal part apparently retained its rapid propulsive motility. Thus, propulsive motility is apparently specific and autonomous in each individual part of the organ.

6322 EFFECT OF VARIOUS GASTROINTESTINAL HORMONES AND VASOACTIVE SUBSTANCES ON VILLOUS MOTILITY. *(E.)* Joyner, W. L.; Kokas, E. (Sch. Med., Univ. North Carolina, Chapel Hill). *Comp. Biochem. Physiol. (A)* 46(1):171-181, 1973.

The effects of i.v. and topical administration of villikinin on villous motility were compared with the effects of other gastrointestinal hormones and vasoactive substances on exteriorized jejunal loops of dogs anesthetized with pentobarbital. Changes in villous motility were expressed by computing the contraction index. The dominant effect of gastrointestinal hormones (secretin, cholecystokinin-pancreozymin, pentagastrin, enterogastrone, and gastric inhibitory peptide) was to inhibit villous motility while human gastrin slightly stimulated it. Vasoactive peptides (cerulein, ranatensin, and eledoisin) inhibited villous motility. Dose-response studies showed that pentagastrin (1.0, 0.5, and 0.1 μg/kg, i.v.) inhibited villous motility at all doses; there was a linear relation between the dose and the contraction index. Cholecystokinin inhibited motility at higher doses (1.0 and 0.5 Ivy U/kg) and stimulated it slightly at a lower dose (0.1 Ivy U/kg). Cerulein inhibited villous motility at all doses (1.0, 0.1, and 0.01 μg/kg, i.v.); a linear relation was found between the log of the dose and the contraction index. At lower doses (0.5, 1.0, 1.5, and 2.0 mg/kg) villikinin stimulated villous motility, while higher doses (2.5 and 5 mg/kg) initially inhibited but then stimulated villous motility. It is concluded that the action of villikinin on villous motility in the small intestine differs from those of the other substances tested.

6323 MEMBRANE PROPERTIES AND INHIBITORY INNERVATION OF THE CIRCULAR MUSCLE CELLS OF GUINEA-PIG CECUM. *(E.)* Ito, Y.; Kuriyama, H. (Fac. Dent., Kyushu Univ., Fukuoka, Japan). *J. Physiol. (Lond.)* 231(3):455-470, 1973.

The membrane properties of the circular muscle cells of guinea-pig cecum and nervous factors influencing the muscle activity were studied with micro-electrodes using partition and field-stimulating methods. The mean membrane potential was -52 mV. Spontaneous discharges appeared as regular bursts between silent periods, as regular spikes without silent period, or as regular slow potential changes with superimposed spikes. Spontaneous spikes with overshoot were frequently observed. The mean maximum rate of rise was 5.2 V/sec. The mean conduction velocity of evoked spikes was 5.4 cm/sec. The amplitude of the electrotonic potential was linearly proportional to the current applied by the partition stimulating method.

The spatial decay of the electrotonic potential along the tissue was exponential, with a mean length constant of 1.7 mm. The time constants of the membrane calculated from the electrotonic potential, and from the conduction velocity, length constant, and time course of the foot of the spike were about 200 and 100 msec resp. These results indicate that the circular muscle of guinea-pig cecum possesses cable-like properties. Field stimulation (0.3 msec pulse duration) to the circular muscle evoked three different responses successively, i.e., initial depolarization (initial excitatory junction potential) with or without spike, hyperpolarization (inhibitory junction otential), and delayed depolarization (delayed excitatory junction potential) with or without spikes. These three different potential changes were completely locked by treatment with tetrodotoxin (5 x 10^{-6} g/ml), and both the initial and late excitatory junction potentials were blocked by treatment with atropine (5 x 10^{-5} g/ml). The distribution of inhibitory nerves in the circular muscle cells was investigated. The results indicate that inhibitory nerves arise from uerbach's plexus situated just beneath the taenia coli and the nerve branches spread over the whole istance from one taenia coli to the next along the circular muscle cells, a width of about 3 mm. The ean conduction velocity of excitation of the inhibitory nerves was 16.0 cm/sec. Hexamethonium, (5 x 10^{-6} g/ml) depolarized the circular muscle membrane nd lowered the rate of rise and fall of spike, but id not block the generation of inhibitory junction otentials. Since hexamethonium did not suppress the nhibitory junction potential, it appears that no ynaptic transmission occurs within the circular musle tissue.

324 INTRACELLULAR RECORDING FROM THE MYENTERIC PLEXUS OF THE GUINEA-PIG ILEUM. *(E.)*

ishi, S.; North, R. A. (Loyola Univ. Med. Ctr., aywood, Ill.). *J. Physiol. (Lond.)* 231(3):471-91, 1973.

ntracellular microelectrodes were used to study anglion cells of the myenteric plexus of the guineaig ileum. Three types of cell were distinguished. ype 1 cells had a high resistance (58 megohms) and ad properties similar to guinea-pig sympathetic anglion cells. Type 2 cells were also excitable ut had a lower resistance (21 megophms) and showed ccommodation to depolarizing current pulses. Type cells were inexcitable. Point stimulation within 50 μm excited neurones either antidromically or rthodromically, sometimes both. Antidromic reponses had a small all-or-nothing component which as subthreshold for the soma spike. Two or more uch components sometimes occurred, and were probaly due to stimulation of 2 or more cell processes. xcitatory postsynaptic potentials were blocked by examethionium (400 μM). They progressively delined in amplitude when elicited at frequencies of .05 Hz or more, and this bears a relation to cetylcholine output. Many cells often showed a low after-hyperpolarization following a direct or ntidromic spike. Spontaneous excitatory postynaptic potentials and spikes were occasionally seen. Intracellular injection of a fluorescent dye revealed that the neurones have 1 to 7 processes, which usually arise from the poles of the oval soma.

6325 COLONIC MOTILITY IN THE CAT II. EXTRINSIC NERVOUS CONTROL. *(E.)*

Rostad, H. (Inst. Neurophysiol., Univ. Oslo, Norway). *Acta Physiol. Scand.* 89(1):91-103, 1973.

The distribution of the extrinsic colonic nerves and their influence on the motility of various parts of the colon were studied in cats lightly anesthetized with penthobarbital sodium and a neuromuscular blocking agent, pancuronium bromide. The motility was recorded in its proximal, middle and distal part with sensitive extraluminal strain gage transducers. Arterial blood pressure and respiratory movements were recorded with pressure transducers. By sectioning of the nerves and by electrical stimulation of the peripheral ends of the cut nerves, the influence of the extrinsic nerves on the colonic motility was investigated. No marked functional differences were noted between the proximal and distal portions of the colon. The vagal and splanchnic nerves, containing pure motor and inhibitory fibers, resp., have their functional distribution throughout the greater part of the colon, although most marked in the proximal part. The parasympathetic pelvic nerves supply the whole colon with motor fibers. The responses in the proximal part of the colon were of lower amplitude and longer latency than in the remaining portions at just suprathreshold stimulation of these nerves. The sympathetic lumbar colonic nerves distribute to all parts of the colon with mainly inhibitory fibers, but have some excitatory fibers as well.

6326 THE MECHANICS OF ESOPHAGEAL MUSCLE CONTRACTION. EVIDENCE OF AN INOTROPIC EFFECT OF GASTRIN. *(E.)*

Cohen, S.; Green, F. (Univ. Pennsylvania Hosp., Philadelphia). *J. Clin. Invest.* 52(8):2029-2040, 1973.

To compare the mechanical properties of lower esophageal sphincter and esophageal circular smooth muscle, force-velocity determinations were made under various physiological conditions. Isotonic and isometric recordings of opossum circular muscle gave the velocity of shortening and force, resp., during changes in: initial muscle length (preload), afterload, calcium concentration, and gastrin I. Muscle contraction to the neurogenic response was elicited at the termination of electrical stimulation. A change in preload altered the peak force developed during an afterloaded contraction, but had only a minor effect on the maximum velocity of shortening. At the length of optimal tension development (preload, 1.5 g), the lower esophageal sphincter muscle had a maximum velocity of shortening of 6.1 mm/sec and a peak force of 17.7 g. The esophageal muscle at its length of optimal tension development (preload 2.0 g) had a maximum velocity of shortening of 6.3 mm/sec and a peak force of 18.1 g. A decrease in calcium from 2.5 to 1.0 mM significantly reduced the maximum velocity of shortening and peak force of all muscle. An increase in calcium to 5.0 mM increased these parameters only minimally. At 1.0 mM calcium, gastrin I increased both maximum velocity of shortening and peak force of all muscle. This inotropic effect of gastrin I occurred at lower concentrations in lower esophageal sphincter muscle than in muscle from the upper esophagus. The power (force X velocity) and work (force X muscle shortening) of esophageal and lower esophageal sphincter muscle were calculated. The work and power generated during esophageal and lower esophageal sphincter muscle contraction were determined by: the initial muscle length as produced by the preload, the afterload against which the muscle was contracting, and the contractility of inotropism of the muscle, i.e., the force-velocity curve on which the muscle was operating.

6327 METOCLOPRAMIDE IN THE VAGOTOMIZED STOMACH. PART II. IN DOG. *(E.)* Kelly, J. M. (Roy. Victoria Hosp., Belfast, Ireland). *Postgrad. Med. J.* 49(4):83-86, 1973.

Metoclopramide (20 mg, i.v., given 3 min after ingestion of food) acted on the gastric antrum in normal dogs, converting the normal pattern of terminal antral contractions to peristaltic emptying waves of high vigor. Within 10 min of administration, the amplitude of the peristaltic waves had reached submaximal values. The action of metoclopramide ceased after 80 min. The effect of metoclopramide on gastric motility or stomach emptying was also studied in the vagotomized dogs. Motility readings were made 1 month after either truncal and selective vagotomy. Truncal vagotomy dramatically decreased overall motility and disorganized the peristaltic waves. Long periods of quiescence were interspersed with bursts of activity. Similar findings were noted after selective vagotomy. In cases where proximal gastric vagotomy had been performed, the overall motility was retained. A few minutes after eating the waves reached their maximal value. No period of terminal antral contraction occurred. Metoclopramide did not alter this pattern of activity as the stomach was already contracting at its maximum amplitude.

6328 EFFECT OF ADRENERGIC RECEPTOR BLOCKADE ON THE RESPONSE TO PROSTAGLANDIN E_1 IN CANINE ILEUM. *(E.)* Kapoor, K.; Levine, R. A. (State Univ. Hosp., Syracuse, N.Y.). *Arch. Int. Pharmacodyn.* 203(2):243-250, 1973.

Prostaglandin E_1 was administered into the blood stream of unanesthetized dogs, each prepared with an ileal fistula. A biphasic motility response consisting of an initial increase in intraluminal pressure followed by prolonged inhibition was induced in the ileum. The responses to protaglandin E_1 were not prevented by pretreatment with phentolamine (5, 10, or 15 mg, i.v.) and propranolol (1 or 15 mg, i.v.), although these 2 adrenoreceptor antagonists inhibited the characteristic relaxant action of epinephrine on intact ileum. Based on the use of these adrenoreceptor blockers, the data suggest that prostaglandin E_1 does not act on adrenergic receptors. Phentolamine, an α adrenergic blocking agent, showed strong contractile effects. Propanolol, a β adrenergic blocker, was without significant effect on intestinal motility.

6329 EFFECT OF INCREASED INTRAPULMONARY PRESSURE ON ELECTRICAL POTENTIALS OF SMOOTH MUSCLES IN THE STOMACH. *(Ukr.)* Lukats'kyi, R. O.; Novos'olova, A. I. (Kherson Pedagogic Inst., USSR). *Dopovidi Akad. Nauk Ukrainsk. RSR* (6):551-552, 1973.

6330 INNERVATION OF THE INTESTINAL MUSCULAR COAT. *(E.)* Gabella, G. (Dept. Anat., Univ. Coll. London, England). *J. Neurocytol.* 1(4): 341-362, 1972.

6331 THE BIOELECTRICAL ACTIVITY OF THE GALLBLADDER, THE ODDI AND LUTCENS SPHINCTERS AND THE STOMACH. *(Rus.)* Klimov, P. K.; Kotelnikova, V. I. (Pavlov Inst. Physiol., Acad. Sci., Leningrad, USSR). *Fiziol. Zh.* 59(1):140-155, 1973.

6332 PHARMACOLOGICAL EFFECTS OF BUTOXYBENZYL HYOSCYAMINE BROMIDE ON THE MOTILITY AND SECRETION OF THE GASTRO-INTESTINAL TRACTS IN ANIMALS. *(Jap.)* Wakabayashi, T.; Yamanaka, T.; Kunii, Y.; Ohgoh, T. (Pharmacol. Res. Labs., Eisai Co. Ltd., Tokyo, Japan). *Folia Pharmacol. Jap.* 69(2):269-283, 1973.

6333 ASSOCIATION OF HYDROMETRIC PROCESSES WITH REGULATION OF THE STOMACH EVACUATION ACTIVITY. *(Rus.)* Korotko, G. F.; Abljazov, A. A. (Med. Inst., Andizhan, USSR). *Fiziol. Zh.* 59(2):337-343, 1973.

6334 THE TACHYPHYLACTIC EFFECT OF BARIUM ON INTESTINAL SMOOTH MUSCLE. *(E.)* Antonio, A.; Rocha e Silva, M.; Yashuda, Y. (Fac. Med., Univ. Sao Paulo, Brazil). *Arch. Int. Pharmacodyn.* 204(2):260-267, 1973.

6335 STUDIES ON THE MUSCARINIC RECEPTOR: pH DEPENDENCE OF THE ACTION OF SOME CHOLINERGIC DRUGS ON THE GUINEA-PIG ILEUM. *(E.)* Jacob, L. S.; Gero, A. (Hahnemann Med. Coll., Philadelphia, Pa.). *Arch. Int. Pharmacodyn.* 204(2):306-315, 1973.

6336 THE EFFECTS OF THEOPHYLLINE AND CYCLIC AMP ON INTESTINAL SMOOTH MUSCLE CONTRAC-

TIONS. *(E.)* Pfaffman, M. A.; McFarland, S. A. (Univ. Mississippi Med. Sch., Jackson). *Eur. J. Pharmacol.* 23(2):147-152, 1973.

6337 THE FUNCTIONAL MECHANISM OF THE BILIARY TRACT (GALLBLADDER AND BILE DUCTS) FROM THE ELECTROBIOLOGICAL STANDPOINT. *(Jap.)* Fujino, T. (Mie Univ. Sch. Med., Japan). *Jap. J. Smooth* *uscle Res.* 8(2):71-84, 1972.

338 STUDIES ON THE LOSS OF ACETYLCHOLINE SENSITIVITY IN ILEAL MUSCLE. *(E.)* oiner, P. D. (Tulane Univ. Sch. Med., New Orleans, a.). *J. Pharmacol. Exp. Ther.* 186(3):552-561, 973.

339 THE EFFECTS OF METOCLOPRAMIDE ON SOME ISOLATED INTESTINAL PREPARATIONS. *(E.)* irtley, R. D. N.; Baines, M. W. (Dept. Pharma- ol., Huntingdon Res. Ctr., England). *Postgrad.* *ed. J.* 49(4):13-18, 1973.

340 GASTRODUODENAL MOTILITY AND SYNCHRONIZATION. *(E.)* Johnson, A. G. (Charing oss Hosp. Med. Sch., London, England). *Post-* *ad. Med. J.* 49(4):29-33, 1973.

41 COMPARISON OF THE EFFECTS OF ORAL AND INTRAVENOUS METOCLOPRAMIDE ON THE SMALL WEL. *(E.)* Pearson, M. C.; Edwards, D.; Tate, A.; lkes, R.; Saxton, H. M.; Howland, C. (Univ. ll. Hosp., London, England). *Postgrad. Med. J.* (4):47-50, 1973.

42 THE ANTI-EMETIC EFFECT OF METOCLOPRAMIDE WITH AN ACCOUNT OF SOME EXPERIMENTS TO SESS THE EFFECT OF THE DRUG ON GASTRIC EMPTYING EARLY LABOUR. *(E.)* McGarry, J. (Welsh Natl. h. Med., Cardiff, Wales). *Postgrad. Med. J.* (4):51-52, 1973.

3 THE RESPONSE OF HUMAN GASTRO-OESOPHAGEAL JUNCTION TO ORALLY ADMINISTERED METO- PRAMIDE. *(E.)* Dilawari, J. B.; Misiewicz, J. (Central Middlesex Hosp., London, England). *tgrad. Med. J.* 49(4):70-71, 1973.

4 ON THE STOMACH SYMPATHETIC PATHWAYS IN RELATION TO ITS MOTOREVACULATORY ACTIVITY. *)* Klimov, P. K.; Nozdratchev, A. D.; ernigovsky, V. N. (Pavlov Inst. Physiol., Acad Sci. USSR., Leningrad). *Fiziol. Zh. SSSR* 59(8):1268-1278, 1973.

6345 STOMACH EMPTYING TIME DETERMINED WITH A PHYSIOLOGICAL MEAL LABELED WITH ^{131}I-ALBUMIN AND ^{99m}Tc-ALBUMIN. *(It.)* Indovina, I.; Scaffidi, L.; Salvia, A. (Inst. Clin. Med., Univ. Palermo, Italy). *Soc. Ital. Biol. Sper.* 48(18): 481-484, 1972.

6346 ELECTROPHYSIOLOGICAL ANALYSIS OF THE GASTRIC SMOOTH MUSCLE FIBER OF GUINEA-PIG AND RABBIT. *(E.)* Kinoshita, S. (Tokyo Med. Coll., Japan). *Tohoku J. Exp. Med.* 110(2): 119-138, 1973.

6347 ANIMAL EXPERIMENTS ON ILEUS OF THE LARGE INTESTINE WITH SPECIAL CONSIDERATION OF LARGE INTESTINE MOTILITY. *(Ger.)* Zlatarski, G.; Willmen, H. R.; Lynen, F. K.; Langer, S.; Heinze, H.; Karhoff, B.; Schweizer, K. (Dept. Surg., Rhine-Westphalian Coll. Technol., Aachen, Germany). *Z. Gastroenterol.* 10(2):114-126, 1972.

6348 IN VIVO STUDY OF THE ELECTRICAL ACTIVITY OF THE COLON IN CHILDREN. *(It.)* Gula, G.; Mollica, F. (Pediatr. Clin., Univ. Catania, Italy). *Pediatria (Napoli)* 80(1):20-42, 1972.

6349 EFFECTS OF INCREASING GLUCOSE CONCENTRATIONS ON THE GLUCOSE METABOLISM IN ARTERIAL TISSUE AND INTESTINAL SMOOTH MUSCLE. *(E.)* Arnqvist, H. J. (Sch. Med., Linkoping, Sweden). *Acta Physiol. Scand.* 88(4):481-490, 1973.

6350 VOMITING AND REFLEX VAGAL RELAXATION OF THE STOMACH ELICITED FROM HEART RECEPTORS IN THE CAT. *(E.)* Abrahamsson, H.; Thoren, P. (Dept. Physiol., Univ. Goteborg, Sweden). *Acta Physiol. Scand.* 88(4):433-439, 1973.

6351 ADENOSINE ANALOGS: STRUCTURE-ACTIVITY RELATIONSHIPS IN VASCULAR AND INTESTINAL SMOOTH MUSCLE. *(E.)* Leslie, S. W.; Borowitz, J. L.; Miya, T. S. (Sch. Pharm. Pharmacal Sci., Purdue Univ., West Lafayette, Ind.). *J. Pharm. Sci.* 62(9):1449-1452, 1973.

6352 EFFECTS OF GASEOUS AIR POLLUTANTS ON GASTRIC SECRETO-MOTOR ACTIVITIES IN THE RAT. *(E.)* Roth, R. P.; Tansy, M. F. (Temple Univ., Sch. Dent., Philadelphia, Pa.). *J. Air Pollut. Control Assoc.* 22(9):706-709, 1972.

6353 N-BUTYL HYOSCINE BROMIDE: ELECTROGASTROENTEROGRAPHIC MONITORING OF GASTROINTESTINAL EFFECTS. *(Fr.)* Martin, A.; Thillier, J. L.; Moline, J.; Levet, E.; Quentin, J. C. (Brettoneau Univ. Hosp. Ctr., Tours, France). *Therapie* 27(3):457-463, 1972.

6354 GASTRIC ELECTROMYOGRAPHY. *(Fr.)* Monges, H.; Salducci, J. (Hop. Nord, Marseille, France). *Arch. Fr. Mal. App. Dig.* 62(5):419-432, 1973.

6355 ACTION OF CERULEIN ON THE LOWER ESOPHAGEAL SPHINCTER IN MAN AND THE DOG. *(Ger.)* Jennewein, H. M.; Siewert, R.; Waldeck, F. (C. H. Boehringer & Son, Ingelheim/Rhein, Germany). *Dtsch. Med. Wochenschr.* 98(7):332-333, 1973.

6356 ACID PERFUSION OF THE ESOPHAGUS AND INTRAGASTRIC PRESSURE. *(Sp.)* Freytes, M. A.; Amuchastegui, L. M.; Madoery, R. (San Roque Hosp., Cordoba, Argentina). *Rev. Esp. Enferm. Apar. Dig.* 39:373-576, 1973.

6357 COLONIC MOTILITY IN THE CAT. I. EXTRALUMINAL STRAIN GAGE TECHNIQUE, INFLUENCE OF ANESTHESIA AND TEMPERATURE. *(E.)* Rostad, H. (Inst. Neurophysiol., Univ. Oslo, Norway). *Acta Physiol. Scand.* 89(1):79-90, 1973.

6358 EXCITATORY AND INHIBITORY EFFECTS OF THE STIMULATION OF THE VAGUS ON THE ELECTRIC ACTIVITY OF THE STOMACH. *(Rus.)* Papasova, M.; Atanasova, E. (Inst. Physiol., Bulgarian Acad. Sci., Sofia). *Fiziol. Zh. SSSR* 59(7):1074-1080, 1973.

6359 STUDIES ON THE INHIBITORY NERVOUS CONTROL OF GASTRIC MOTILITY. *(E.)* Abrahamsson, H. (Dept. Physiol., Univ. Goteborg, Sweden). *Acta Physiol. Scand.* (Suppl. 390):1-38, 1973.

6360 EFFECT OF PROXIMAL GASTRIC, COMPLETE GASTRIC, AND TRUNCAL VAGOTOMY ON CANINE GASTRIC ELECTRIC ACTIVITY, MOTILITY, AND EMPTYING. *(E.)* Wilbur, B. G.; Kelly, K. A. (Mayo Clin., Rochester, Minn.). *Ann. Surg.* 178(3):295-303, 1973.

See also, 6282, 6313, 6804, 6806, 6935, 6940, 7020, 7186.

SECRETION AND METABOLISM

6361 INTERRELATIONS OF HUMORAL AND CELLULAR IMMUNE RESPONSES IN EXPERIMENTAL CANINE GASTRITIS. *(E.)* Krohn, K. J. E.; Finlayson, N. D. C. (Dept. Pathol., Univ. Helsinki, Finland). *Clin. Exp. Immunol.* 14(2):237-245, 1973.

In this study 8 mongrel dogs immunized intradermally with autologous or homologous gastric juice in Freund's complete adjuvant developed gastritis, whereas 4 mongrel dogs immunized with the adjuvant alone did not. Gastric changes occurred in all dogs in the course of immunization. The first change was infiltration of chronic inflammatory cells in superficial layers of the lamina propria. Further immunization spread the inflammatory cell infiltration to the area of the glands containing parietal and chief cells. A focal fibrotic reaction with degenerative changes in parietal and chief cells was seen later. Cellular immunity to gastric juice antigens, demonstrated by skin testing and peripheral leucocyte migration inhibition, coincided with the appearance of gastritis, whereas parietal cell antibodies appeared some 2 weeks later. The work demonstrates the combined humoral and cellular immune response of the dogs to gastric juice, and suggests that the cellular response may be of primary importance in the development of gastritis.

6362 EFFECT OF RADIATION ON GASTRIC SECRETION IN THE RAT AND THE RADIOPROTECTIVE ACTION OF ATP. *(Fr.)* Groza, P.; Gheorghe, N.; Stefan, M. (no affil.). *Rev. Roum. Physiol.* 10(1):3-11, 1973.

Gastric secretion and ATPase activity in the rat gastric mucosa were investigated 30 min to 15 days after exposure to a single dose of 500 r radiation.

A few hours after irradiation, the volume of gastric juice decreased to about 1/2 of its initial value, increasing to larger than normal values on day 5. Except for the first few hours, when free acidity decreased to zero, total and free acidity increased progressively during the first 5 days after irradiation; normalization occurred after 15 days. For the first 5 days after irradiation, both total acid output and pepsin activities were increased. ATPase activity in the gastric mucosa first decreased but returned to normal levels after 3 hr. When administered 30 min before irradiation, ATP [dose unspecified] had a radioprotective action, decreasing both total acidity and acid output. ATP also increased ATPase and decreased pepsin activity in the first few hours after irradiation. These findings suggest that ATP plays a role in the synthesis of acid in the stomach.

363 DIFFERENTIATION OF PEPSINOGEN-PRODUCING CELLS IN THE FUNDIC AND PYLORIC MUCOSA OF
EVELOPING RATS. *(E.)* Furihata, C.; Iwasaki, Y.;
ugimura, T.; Tatematsu, M.; Takahashi, M. (Inst.
ed. Sci., Univ. Tokyo, Japan). *Cell Different.*
(3):179-189, 1973.

he peptic activity in the fundic mucosa of Wistar
ats increased significantly between the 18th and
0th days of life. The peptic activity in the pyloric
ucosa remained constant after birth. Electrophoresis
f pepsinogen from the fundic mucosa indicated that
aturation of the fundic mucosa begins at least at
ay 13 and is completed by day 25 or 30. Electro-
horesis revealed a band between Bands I and II, in-
icating that other bands besides I, II, and III are
roduced in the chief cells. Morphological studies
ndicated that mature chief cells began to appear
round 16-17 days after birth and the secretory
ranules in the cells increase in size and number
that time. The chief cells had matured by day
-25. The endoplasmic reliculum was poorly developed
the chief cells until about 18-25 days after birth
en it rapidly matured. The lack of change in the
ptic activity, molecular species of pepsinogen,
the morphology of pyloric gland cells in the rat
loric mucosa after birth suggests that pyloric
and cells are mature at birth. These results in-
cate that pepsinogens are mainly synthesized in
e chief cells in the fundic mucosa of mature rats.

64 THE EFFECT OF GASTRIN ON BASAL- AND GLUCOSE-STIMULATED INSULIN SECRETION IN MAN. *(E.)*
hfeld, J. F.; Stadil, F. (Bispebjerg Hosp., Copen-
gen, Denmark). *J. Clin. Invest.* 52:1415-1426,
73.

e effect of gastrin on basal- and glucose-stimulated
sulin secretion was studied in 32 normal subjects
4 males and 8 females, 24-42 yr old). Maximal
ysiologic limit for the concentration of gastrin
serum was of the order of 160 pmol/liter as observed during a protein-rich meal. Oral ingestion of 50 g glucose produced a small gastrin response from 28 to 39 pmol/liter. I.v. injection or prolonged infusion of gastrin increased the concentration of insulin in peripheral venous blood to a maximum within 2 min followed by a decline to basal levels after a further 10 min. The minimum dose required to induce a significant insulin response (31.2 ng gastrin/kg) increased the gastrin level in serum above the physiologic range. Maximum effect was obtained with 500 ng gastrin/kg. When 15.6 ng (7.1 pmol) gastrin/kg and 25 g glucose were injected simultaneously, the glucose-induced insulin response was potentiated (from 2.32 to 4.33 nmol/liter/20 min), even though gastrin concentrations only increased to 71.2 pmol/liter. No effect was noted on glucose disposal. Gastrin (15.6 ng/kg, i.v.) given 30 min before an i.v. glucose tolerance test did not affect the insulin response. Thus, gastrin can stimulate a rapid and short-lived release of insulin. In physiologic concentrations gastrin potentiates the glucose-stimulated insulin secretion and is without effect on basal insulin secretion. A small release of gastrin during oral glucose ingestion may to a limited extent contribute to the nonglycemic insulin secretion. During protein ingestion, gastrin probably stimulates insulin secretion significantly.

6365 ABO SALIVA AND PLASMA AGGLUTININS IN TWINS. *(E.)* Callegari, S. M.; Salzano, F. M.; Pena, H. F. (Inst. Biosci., Federal Univ. Rio Grande Sul, Porto Alegre, Brazil). *Acta Genet. Med. Gemellol. (Roma)* 21(4):287-296, 1972.

6366 ABH SALIVARY SECRETION IN TWINS. *(E.)* Callegari, S. M.; Salzano, F. M.; Pena, H. F. (Inst. Biosci., Federal Univ. Rio Grande Sul, Porto Alegre, Brazil). *Acta Genet. Med. Gemellol. (Roma)* 21(4):297-304, 1972.

6367 SALIVARY REACTIONS AFTER VENTROMEDIAL HYPOTHALAMIC LESIONS IN DOGS. *(E.)* Rozkowska, E.; Fonberg, E. (Nencki Inst. Exp. Biol., Warsaw, Poland). *Acta Neurobiol. Exp.* 33(2):553-562, 1973.

6368 HANDLING OF WATER AND ELECTROLYTES BY RABBIT PAROTID AND SUBMAXILLARY GLANDS. *(E.)* Mangos, J. A.; McSherry, N. R.; Irwin, K.; Hong, R. (Univ. Wisconsin Med. Sch., Madison). *Am. J. Physiol.* 225(2):450-455, 1973.

6369 INTERRELATIONSHIP BETWEEN AMINO ACID POOLS AND PROTEIN SYNTHESIS IN THE RAT SUBMANDIBULAR GLAND. *(E.)* Van Venrooij, W. J.;

Kuijper Lenstra, A. H.; Kramer, M. F. (Fac. Med., Natl. Univ., Utrecht, Netherlands). *Biochim. Biophys. Acta* 312(2):392-398, 1973.

6370 NEURONAL AND HORMONAL INFLUENCES ON THE TURNOVER OF MONOAMINE OXIDASE IN SALIVARY GLAND. *(E.)* Goridis, C.; Neff, N. H. (Lab. Preclin. Pharmacol., NIH, Washington, D.C.). *Biochem. Pharmacol.* 22(20):2501-2510, 1973.

6371 INHIBITORY EFFECT OF ISOPRENALINE ON ENTRY OF CELLS INTO S PHASE IN THE RAT SUBMAXILLARY GLAND. *(E.)* Radley, J. M.; Hodgson, G. S. (Cancer Inst., Melbourne, Victoria, Australia). *Aust. J. Exp. Biol. Med. Sci.* 51(3):399-404, 1973.

6372 THE EFFECT OF ISOPRENALINE AND PILOCARPINE ON (a) BRONCHIAL MUCUS-SECRETING TISSUE AND (b) PANCREAS, SALIVARY GLANDS, HEART, THYMUS, LIVER AND SPLEEN. *(E.)* Sturgess J.; Reid, L. (Brompton Hosp., London, England). *Br. J. Exp. Pathol.* 54(4):388-403, 1973.

6373 CYCLIC ADENOSINE 3',5'-MONOPHOSPHATE CONCENTRATION IN RABBIT PAROTID SLICES FOLLOWING STIMULATION BY SECRETAGOGUES. *(E.)* Monnard, P.; Schorderet, M. (Inst. Pharmacol., Med. Sch., Geneva, Switzerland). *Eur. J. Pharmacol.* 23(3):306-310, 1973.

6374 ISOTOPES IN THE FUNCTIONAL DIAGNOSIS OF THE PAROTID. I. FUNCTION OF THE NORMAL PAROTID. *(Ger.)* Hug, I.; (Canton Hosp., Basel, Switzerland). *Fortschr. Rontgenstr.* 119(2):165-174, 1973.

6375 SOURCE OF NEURAMINIDASE IN HUMAN WHOLE SALIVA. *(E.)* Fukui, Y.; Fukui, K.; Moriyama, T. (Hiroshima Univ. Sch. Dentistry, Japan). *Infect. Immun.* 8(3):329-334, 1973.

6376 ABSENCE OF A NEURALLY-MEDIATED PROCESS IN SALIVATION AND VASODILATION CAUSED BY McN-A-343 IN THE DOG SUBMAXILLARY GLAND. *(E.)* Satoh, S.; Taira, N.; Hashimoto, K. (Akita Univ. Sch. Med., Japan). *Jap. J. Pharmacol.* 23(4):581-583, 1973.

6377 SALIVARY ELECTROLYTES, RENIN, AND ALDOSTERONE DURING SODIUM LOADING AND DEPLETION. *(E.)* Wotman, S.; Baer, L.; Mandel, I. D.; Laragh, J. H. (Coll. Phys. Surg., Columbia Univ., New York, N.Y.) *J. Appl. Physiol.* 35(3):322-324, 1973.

6378 EXPERIMENTAL PROTEIN-CALORIE MALNUTRITION IN THE GUINEA PIG AND EVALUATION OF THE ROLE OF ASCORBIN ACID STATUS. *(E.)* Enwonwu, C. O. (Ctr. Res. Oral Biol., Univ. Washington, Seattle). *Lab. Invest.* 29(1):17-26, 1973.

6379 PROSTAGLANDIN $F_{2\alpha}$ AS A POTENT EXCITANT OF THE PARASYMPATHETIC POSTGANGLIONIC NEURONS OF THE DOG SALIVARY GLAND. *(E.)* Taira, N.; Satch, S. (Tohoku Univ. Sch. Med., Sendai, Japan). *Life Sci.* 13(5):501-506, 1973.

6380 COORDINATION OF THE DIGESTIVE SEQUENCE. *(E.)* Go, V. L. W. (Mayo Clin., Rochester, Minn.). *Mayo Clin. Proc.* 48(9):613-616, 1973.

6381 ADVANCES IN GASTROINTESTINAL ENDOCRINOLOGY. *(E.)* Konturek, S. (Med. Acad., Cracow, Poland). *Pol. Endocrinol.* 23(5):329-341, 1972.

6382 ANALOGOUS MODEL OF GRADIENT OF THE SMALL INTESTINE ACTIVITY. *(Rus.)* Reshodko, L. V.; Illin, N. N.; Bogach, P. G. (Kiev State Univ., USSR). *Fiziol. Zh. SSSR.* 59(5):808-813, 1973.

6383 STEROID METABOLISM BY MOUSE SUBMAXILLARY GLANDS. I. IN VITRO METABOLISM OF TESTOSTERONE AND 4-ANDROSTENE-3,17-DIONE. *(E.)* Coffey, J. C. (Dental Res. Ctr., Univ. North Carolina, Chapel Hill.). *Steroids* 22(2):247-257, 1973.

6384 RADIATION-INDUCED HYPERAMYLASEMIA. *(Rum.)* Olinescu, R.; Nita, S.; Muntiu, M.; Costea, L. (Fundeni Clin. Hosp., Bucharest, Rumania). *Stud. Cercet. Biochim.* 16(1):45-51, 1973.

6385 AGE CHANGES IN ALKALINE AND ACID PHOSPHATASE ACTIVITY OF SALIVA AND SALIVARY GLANDS IN RATS. *(Rus.)* Marchenko, A. I.; Levytsky, A. P.; Barabash, R. D. (Res. Inst. Stomatol., Odessa, USSR). *Ukr. Biokhim. Zh.* 45(3):307-311, 1973.

6386 INFLUENCE OF A SUCROSE DIET ON THE AMINOTRANSFERASE AND PHOSPHATASE ACTIVITY IN THE SALIVA OF RATS OF DIFFERENT AGE. *(E.)* Petrovich, Y. A.; Podorozhnaya, R. P. (Moscow Med. Stomatol. Inst., USSR). *Vopr. Pitan.* (2):54-56, 1973.

See also, 6298, 6300, 6332, 6494.

SECRETION AND METABOLISM

Stomach

;387 PROTECTIVE EFFECT OF PROSTAGLANDIN E_1 (PGE_1) ON LYSOSOMAL ENZYME RELEASE IN SERO-
TONIN-INDUCED GASTRIC ULCERATION. *(E.)* Ferguson,
V. W.; Edmonds, A. W.; Starling, J. R.; Wangensteen,
S. L. Univ. Virginia Sch. Med., Charlottesville).
Inn. Surg. 177(6):648-654, 1973.

'rostaglandin E_1 (75 µg/kg, s.c.) and serotonin
(60 mg/kg, i.p.) were used in male Sprague-Dawley
ats. Prostaglandin diluent and serotonin diluent
vere also employed. Rats receiving serotonin and
rostaglandin E_1 diluent had 2.8 ulcers/stomach
ompared with 0.7 in those receiving both serotonin
nd prostaglandin E_1. Neither prostaglandin E_1 nor
erotonin diluent alone caused gastric ulcerations.
n rats receiving both serotonin and prostaglandin
1, the stomach of cathepsin D was 17.4 U/mg protein,
ompared to 13.4 in rats receiving serotonin, and
6.1 in rats receiving only prostaglandin E_1. Pros-
aglandin E_1 lowered plasma cathepsin D activity
ignificantly (3.9 U/ml) compared to diluent-treated
ontrols (5.6 U/ml). Plasma cathepsin D was 10.0
/ml in serotonin-treated rats. Prostaglandin E_1
id not prevent the rise in cathepsin activity in
ats receiving both serotonin and prostaglandin E_1.
he rise due to serotonin was marked at 1 hr, and
eclined toward control levels in 6 hr. Serotonin
aused the rats to become markedly cyanotic, pros-
rate, and have difficulty breathing. Prostaglandin
did not modify these reactions. The pH of the
astric washings of rats receiving prostaglandin E_1
s 4.2 *versus* 3.6 rats receiving only serotonin
luent, thus indicating that prostaglandin E_1
hibits gastric secretion. Prostaglandin E_1 en-
nced lysosomal stability in challenge by heat and
itation in 0.25M sucrose, whether tested *in vivo*
in vitro. Results of tncubation of lysosomal
zyme extracts with dog erythrocytes showed a linear
lation between cathepsin D activity in the lysoso-
l extract and the amount of hemoglogin release;
is indicated that the enzymes lysed erythrocytes,
esumably by direct hydrolytic action on the cell
mbrane. Thus, lysosomal enzymes may be important
serotonin-induced ulceration pathogenesis.

6388 EFFECT OF PENTAGASTRIN, HISTAMINE, AND CYCLIC 3',5'-AMP ON CARBONIC ANHYDRASE ACTIVITY IN THE GASTRIC MUCOSA OF THE RAT. *(Rus.)* Salganik, R. I.; Argutinskaia, S. V.; Bersimbaev, R. I.; Zimonina, T. V. (Inst. Cytol. Genetics, Novosibirsk, USSR). *Biokhimiia* 38(1):174-177, 1973.

Carbonic anhydrase activity in the gastric mucosa of fasting Wistar rats more than doubled 60 min after administration of pentagastrin (2 doses of 0.4 µg/100 g each, given s.c. at 20-30 min intervals) or histamine (200 µg/100 g i.m.). Administration of actinomycin D (100 µg/100 g) 30 min before and 30 min after pentagastrin or i.p. injection of cycloheximide (70 µg/100 g) or ethionine (30 µg/100 g) 30 min before pentagastrin injection completely suppressed activation of carbonic anhydrase activity by pentagastrin. None of these inhibitors of DNA-dependent RNA synthesis had any effect on increased carbonic anhydrase activity induced by histamine. Administration of 3',5'-AMP or dibutyryl 3',5'-AMP (5 mg/100 g i.p.) increased carbonic anhydrase activity, which increased still further with simultaneous administration of theophylline (5 mg/100 g i.p.). Actinomycin D and cycloheximide had no effect on carbonic anhydrase activation induced by 3',5'-AMP. These findings confirm that activation of carbonic anhydrase by 3',5'-AMP and histamine is not related to increased DNA-dependent synthesis of RNA and proteins. It is suggested that HCl secretion in the stomach is regulated as follows: gastrin activates DNA-dependent RNA synthesis in the gastric mucosa, ensuring production of histidine decarboxylase and thus the production of histamine. Histamine activates adenyl cyclase and the 3',5'-AMP formed activates carbonic anhydrase which is responsible for HCl production.

6389 EFFECT OF CAERULEIN AND ENDOGENOUS CHOLECYSTOKININ ON URECHOLINE-INDUCED GASTRIC ACID

AND PANCREATIC PROTEIN SECRETION IN DOGS. *(E.)* Konturek, S. J.; Tasler, J.; Obtulowicz, W. (Med. Acad., Cracow, Poland). *Gastroenterology* 65(2):235-241, 1973.

Dogs with vagally innervated Pavlov pouches (PP), gastric fistulae, and pancreatic fistulae were studied. Added to a background of bethanechol chloride infusion (100 μg/kg/hr), caerulein (30-250 ng/kg/hr) increased PP response with the maximum reaching about 80% of the maximal response to histamine dihydrochloride (320 μg/kg/hr) and 55% of the maximal response to a meat meal of 25 g/kg. Endogenous cholecystokinin, released intraduodenal instillation of amino acids, produced pancreatic protein output similar to that obtained with caerulein at the dose of 120 ng/kg/hr, and resulted in bethanechol chloride-induced acid secretion reaching about 50% of the maximal response to histamine. After surgical conversion of PP to Heidenhain pouches (HP), the addition of caerulein to background bethanechol chloride stimulation resulted in dose-related increases in acid output from the HP, reaching, at the highest side effect-free dose of caerulin (250 ng/kg/hr), about 170% of the maximal response to histamine and about 180% of the response to feeding. The highest pancreatic protein outputs in response to various doses of caerulein, or intraduodenal amino acids, combined with bethanechol chloride were significantly higher than those in response to caerulein or amino acids alone. The peak responses to these combinations were comparable to those obtained with a meat meal and did not change after transformation of PP to HP. Thus the combination of cholecystokinin and cholinergic drug increases gastric acid and pancreatic protein secretion, particularly in vagally denervated gastric pouches.

6390 METABOLISM OF PROSTAGLANDIN E_1 IN STOMACH, JEJUNUM CHYLE AND PLASMA OF THE DOG AND THE RAT.

(E.) Nakano, J.; Prancan, A. V.; Morsy, N. H. (Univ. Oklahoma Sch. Med., Oklahoma City). *Jap. J. Pharmacol.* 23(3):355-361, 1973.

The metabolic degradation of prostaglandin E_1 was studied by incubating ^{3}H-prostaglandin E_1 with rat and dog plasma and thoracic lymph and the homogenates of various rat and dog tissues. Rat and dog plasma metabolized very little prostaglandin E_1 even when incubated for 1 hr. Very little metabolic degradation of prostaglandin E_1 was found by dog thoracic lymph. In contrast, rat and dog lung and kidney metabolized prostaglandin E_1 very rapidly, and approximately 95% of prostaglandin E_1 was converted to a less polar metabolite within 20 min of incubation. The metabolic degradation of prostaglandin E_1 was also rapid in the homogenates of rat stomach and jejunum, but the velocity of this reaction in these homogenates was slower than that in the rat or dog lung and kidney homogenates. These results suggest that the administration of prostaglandins p.o. may not be as effective in reducing gastric acidity as in i.v. administration.

6391 EFFECTS OF GASTRIC ACID STIMULANTS AND INHIBITORS ON THE ACTIVITIES OF HCO_3^--STIMULATED Mg^{2+}-DEPENDENT ATPASE AND CARBONIC ANHYDRASE IN RAT GASTRIC MUCOSA.

(E.) Narumi, S.; Kanno, M. (Biol. Res. Lab., Takeda Chem. Industries, Osaka, Japan). *Biochim. Biophys. Acta* 311(1):80-89, 1973.

An investigation was made of the *in vivo* and *in vitro* effects of gastric acid stimulants and inhibitors on the activities of HCO_3^--stimulated ATPase (HCO_3^--ATPase), Mg^{2+}-dependent ATPase (Mg^{2+}-ATPase), and carbonic anhydrase in rat gastric mucosa. Carbachol (25-400 μg/kg, s.c.) induced gastric juice secretion in 3-hr pylorus-ligated Sprague-Dawley rats. This drug also increased the activities of Mg^{2+}-ATPase and carbonic anhydrase in homogenates of rat gastric mucosa. Gastric acid stimulants, i.e. carbachol (25 400 μg/kg, s.c.), gastrin 50-400 μg/kg, s.c.), and histamine (0.5-8 mg/kg, s.c.), stimulated gastric juice secretion in 3-hr pylorus-ligated rats and increased the Mg^{2+}-ATPase and carbonic anhydrase activities in the mitochondrial fraction of rat gastric mucosa. Pretreatment with atropine (5 mg/kg, s.c.) or acetazolamide (20 mg/kg, s.c.) prevented the carbachol-induced increase in the activities of Mg^{2+}-ATPase and carbonic anhydrase in the mitochondrial fraction. Incubation of Mg^{2+}-ATPase or HCO_3^--ATPase *in vitro* with histamine (10^{-3}M), carbachol (10^{-3}M), or tetragastrin (10^{-5}M) had no effect on enzyme activity. These reagents did not directly stimulate enzyme activity. Thiocyanate (10^{-2}M) inhibited enzyme activity about 30-40%, while ouabain (10^{-2}M) had no effect on the activity. These findings indicate that Mg^{2+}-ATPase and carbonic anhydrase activities in the mitochondrial fraction of gastric mucosa are correlated with gastric acid secretion. It is probable that carbonic anhydrase is functionally linked to Mg^{2+}-ATPase in rat gastric mucosa.

6392 HISTAMINE METABOLISM IN HUMAN GASTRIC MUCOSA.

(E.) Dencker, H.; Kahlson, G.; Kockum, I.; Norryd, C.; Rosengren, E. (Inst. Physiol., Univ. Lund, Sweden). *Clin. Sci. Mol. Med.* 45(2):225-231, 1973.

Gastric mucosa specimens from 7 patients operated on for peptic ulcer (4) or early carcinoma (3) were examined. The histamine-forming capacity, i.e., present. The histamine-forming capacity, i.e., histidine decarboxylase activity, in the acid-secreting mucosa was studied by a highly sensitive and specific isotope-dilution method. Activity was observed in each of 6 specimens so studied. The enzyme, histamine methyltransferase, which methylates ring nitrogen, was also present and the product, which is inactive as a gastric acid secretogogue, was observed. Ring methylation appears to be an effective means of protecting the systemic circulation from histamine which is known to affect blood vessels and smooth muscles, even in very small concentrations. The products of side-chain *N*-methylation, *N*-methylhistamine and *N*-dimethyl histamine, both of which are highly active in promoting acid secretion, could not be detected by biological and chromatographic techniques.

6393 FAILURE OF SC-19220 TO AFFECT PROSTAGLANDIN E_1 (PGE_1) GASTRIC ANTISECRETORY ACTIONS.

E.) Engel, J. J.; Scruggs, W.; Wilson, D. E. (Dept.
ed., Univ. Illinois, Chicago). *Prostaglandins* 4(1):
5-70, 1973.

he effects of 1-acetyl-2-(8-chloro-10,11-dihydro-
ibenz(b,f)(1-4)oxazepine-10-carbonyl)hydrazine on
rostaglandin E_1-induced inhibition of gastric secre-
ion *in vivo* in pylorus-ligated rats have been tested.
his compound did not effect gastric secretion alone
n concentrations of 250 or 500 µg/kg. However, when
sed in concentrations greater than 1000 µg/kg, gas-
ric secretion was depressed perhaps due to the
ction of the compound as a partial agonist or due
o central nervous system depression. At these higher
oncentrations, erratic behavior and convulsions were
requently noted. Prostaglandin E_1 (250 µg/kg) sig-
ificantly reduced gastric juice volume, acid output
d acid concentration. The additional administra-
on of 250 µg/kg of 1-acetyl-2-(8-chloro-10,11-di-
drobenz(b,f)(1-4)oxazepine-10-carbonyl)hydrazine
d not change these effects. Selective inhibition
some prostaglandin actions by antagonists may be
clinical importance in efforts to develop a pros-
glandin or analogue with significant gastric anti-
cretory effects which does not have uncomfortable
de effects on gastrointestinal motility.

394 RELEASE OF GASTRIN BY EPINEPHRINE IN MAN.

(E.) Stadil, F.; Rehfeld, J. F. (Rigshosp.,
penhagen, Denmark). *Gastroenterology* 65(2):210-
5, 1973.

8 normal subjects infusion of epinephrine (25-75
/kg/min, i.v., for 10 min) significantly increased
rum concentration of gastrin and acid secretion.
e increase in gastrin concentration (from a mean
out 45 to 90 to 110 pg/ml of serum) was prompt, and,
ke the increase in acid, of short duration. Marked
fferences in the response were found among the 8
dividuals. Doses of 125 and 150 ng of epinephrine/
/min, given to 1 subject, lowered serum gastrin
ncentration. Prior administration of pindolole (500
/kg/min), a β adrenergic blocking agent, completely
ppressed the effect on serum gastrin concentration
acid secretion. Some anxiety and discomfort was
perienced by most of the subjects; 1 subject suf-
red severe discomfort.

95 THE EFFECT OF ORALLY AND INTRAVENOUSLY ADMINISTERED PROSTAGLANDIN 16:16 DIMETHYL METHYL ESTER ON HUMAN GASTRIC ACID SECRETION.

) Karim, S. M. M.; Carter, D. C.; Bhana, D.;
esan, P. A. (Makerere Univ. Med. Sch., Kampala,
nda). *Prostaglandins* 4(1):71-83, 1973.

staglandin 16:16 E_2 methyl ester (25-200 g, p.o.)
administered to 7 healthy male volunteers. In
f these subjects, gastric juice pH rose above
after administration of 50 µg of the analogue; this fall in acidity was sustained in 3 subjects for more than 75 min. All 5 subjects receiving the 200 µg dose showed a sharp rise in pH, which was sustained above pH 6 for the remainder of the 3 hr aspiration. When the analogue was administered i.v., (3.125 µg to 50 µg), a 30 min rise to pH 5.0 was noted on injection of the 6.25 µg dose level. Prostaglandin administered i.v. or p.o. also inhibited acid secretion stimulated by pentagastrin (6 µg/kg, i.m.). It is suggested that the inhibition likely resulted from a direct action on the parietal cell, possibly related to the adenyl cyclase enzyme system. The ability of the analogue to reduce gastric secretion when given i.v., may be of great value in treating the problems of hemorrhagic gastritis and bleeding peptic ulceration.

6396 THE EFFECT OF SECRETIN ON GASTRIC EMPTYING AND SECRETION IN MAN.

(E.) Ramsbottom, N.; Hunt, J. N. (Guy's Hosp., London, England). *Rend. Gastroenterol.* 5(1):6-12, 1973.

In 2 healthy male subjects continuous i.v. infusions of large amounts of secretin (22, 45, or 90 clinical U/20 min) slowed the gastric emptying of rapidly emptying meals (100 mN sodium citrate). The same amounts of secretin did not slow the gastric emptying of slowing emptying test meals (50 g/liter of glucose monohydrate or 30 mN HCl). The same infusions of secretin apparently inhibited the outputs of acid and of chloride in response to all 3 meals, despite the fact that glucose and acid meals were effective inhibitors of secretion in their own right. The results suggest that secretin, in large amounts, is a weak inhibitor of gastric emptying; strong inhibition of gastric emptying by glucose or acid is not mediated by secretin; and that secretin, in large amounts, is an effective inhibitor of gastric secretion, even when it is already inhibited by glucose or by acid.

6397 VAGAL STIMULATION, GASTRIN RELEASE, AND ACID SECRETION IN ANESTHETIZED DOGS.

(E.) Lanciault, G.; Bonoma, C.; Brooks, F. P. (Univ. Pennsylvania Sch. Med., Philadelphia). *Am. J. Physiol.* 225(3):546-552, 1973.

Electrical stimulation was applied to the distal cut ends of the vagi of anesthetized dogs. Gastric juice was collected from a gastric fistula. Immunoreactive gastrin levels were determined on portal and femoral venous blood. Intermittent stimulation of the vagi consistently elevated portal serum gastrin levels (3-4-fold); however, acid output rose regularly only after the first stimulation. Constant stimulation of the vagi up to 4 hr elevated both portal serum gastrin and acid output. Midcollicular decerebration increased basal and stimulated levels of gastrin, but acid output was unchanged. Antrectomy or isolation of the antrum along with vagal stimulation, reduced gastrin levels and acid output to control levels. Perfusion of an antral pouch with phosphate-buffered saline at pH 7.0 produced no change in gastrin or acid output. With 0.1 N HCl, portal gastrin levels fell to prestimulated levels, although acid output remained elevated. Cutting the vagi produced a tachycardia which fell to or below control levels with vagal stimulation. No significant changes occurred in mean arterial and portal blood pressure. Electrical stimulation of the vagi produced predictable changes in portal serum gastrin, which were blocked by antrectomy and/or antral isolation, and perfusion of the antrum with HCl. Responses of acid output were less consistent and, on occasion, independent of changes in portal serum gastrin.

6398 SIMULTANEOUS ELECTROPHORESIS OF PEPSINOGENS AND PEPSINS.

(E.) Mangla, J. C.; Guarasci, G.; Turner, M. D. (Univ. Rochester Sch. Med., N.Y.). *Am. J. Dig. Dis.* 18(10):857-864, 1973.

Buffer systems with a pH 8.3 and a pH 5.7 for agar gel electrophoresis of human pepsinogens and pepsins were prepared. Electrophoresis of pepsinogens and pepsins was performed on the same plate with the pH 5.7 buffer, and relations of the major enzyme and zymogen components were determined. Four major and 7 minor zymogen bands were found by electrophoresis of extracts of human gastric mucosa. On activation of these extracts with 0.5 N HCl, the number of enzymatically active bands remained the same, although their mobility was increased. On two-dimensional electrophoresis, the relation of 4 major bands was maintained after activation. The most mobile pepsin was derived from the most mobile pepsinogen, the least mobile pepsin from the least mobile pepsinogen, and intermediate pepsins from corresponding intermediate pepsinogens.

6399 THE GASTRIC MUCOSAL RESPONSE TO ACETYLSALICYLIC ACID IN THE FERRET. AN ULTRASTRUCTURAL STUDY.

(E.) Pfeiffer, C. J.; Weibel, J. (Fac. Med., Memorial Univ. Newfoundland, St. John's, Canada). *Am. J. Dig. Dis.* 18(10):834-846, 1973.

The acute gastric mucosal, morphologic response to orally ingested acetylsalicylic acid was studied by electron microscopy in adult fasted ferrets. A single, clinically relevant dose (10 mg/kg) was administered and gastric surface responses were studied by scanning electron microscopy. Differential early, cytologic responses of the glandular cells were evaluated by transmission electron microscopy. Gastric bleeding was derived from minute, surface erosions morphologically identical with stress-type erosions. Parietal cells underwent drug-specific changes, and chief cells underwent nonspecific degenerative changes. Only localized disruption of mucous epithelial cells occurred. Tight junctions between surface epithelial cells remained intact. The order of decreasing cellular sensitivity to this acute (10-45 min) exposure to hydrochloric acid-acidified aspirin solution was: parietal cells, chief cells, and surface epithelial cells. Argentaffin cells and mucous neck cells were resistant.

6400 ADAPTATION OF THE GASTRIC MUCOSA TO REPEATED ADMINISTRATION OF ASPIRIN IN THE RAT.

(E.) St. John, D. J. B.; Yeomans, N. D.; McDermott, F. T.; de Boer, W. G. R. M. (Monash Univ. Dept. Med., Melbourne, Australia). *Am. J. Dig. Dis.* 18(10):881-886, 1973.

The effects of single and repeated doses of aspirin on the gastric mucosa of male Sprague-Dawley rats were compared. Aspirin (120 mg/kg) was administered by esophageal intubation either as a single dose or daily for 3, 14, 28, or 56 days. Mucosal damage was present in all rats but, there was a highly significant reduction in the number of acute erosions in those receiving repeated daily aspirin. This adaptation did not persist when administration of the aspirin was interrupted for 3 days. Repeated aspirin administration was not associated with any reduction in aspirin absorption or excretion, nor was there any significant change in hydrochloric acid or pepsin secretion. Thus an adaptation to repeated aspirin apparently occurs in the rat which probably results from an alteration in the gastric mucosa. Increased resistance to aspirin-induced damage could be related to the presence of substantial areas of regenerating mucosa, but other possibilities such as the induction of drug-metabolizing enzymes must also be considered.

6401 DUODENAL INHIBITION OF GASTRIC ACID SECRETION.

(E.) Andersson, S. (Dept. Pharmacol., Karolinska Inst., Stockholm, Sweden). *Acta Hepatogastroenterol.* 19(6):458-463, 1972.

In dogs with gastric and pancreatic fistulae the effect of acidification of isolated duodenal bulb pouches was studied on gastric and pancreatic secretions. Acidification of the duodenal bulb with 0.1 N HCl produced significant inhibition of gastric acid output in response to pentagastrin (12.5 µg/hr) without detectable stimulation of pancreatic volume and enzyme output. Secretin (0.25 and 0.50 U/kg/hr) administered during continuous infusion of pentagastrin, caused significant stimulation of pancreatic secretion with no inhibitory effect on gastric secretion. In postbulbar acidification, gastric secretion was stimulated with pentagastrin. Infusion of 0.1 N HCl in the postbulbar duodenum caused great secretory response from the pancreas, but only a weak inhibition of the gastric secretion was observed. These results support existing evidence for a specific inhibitory substance released from the duodenal bulb mucosa by acid. It is not likely that gastric inhibition following bulbar acidification was caused by the release of cholecystokinin-pancreozymin, for no increase of amylase concentration was observed in the pancreatic juice during duodenal acidification.

6402 PREVENTION OF ASPIRIN-INDUCED GASTRIC ULCERATION IN RATS BY α-METHYLDOPA AND DISUL-
FIRAM. *(E.)* Hemmati, M.; Rezvani, A.; Djahanguiri,
B. (Fac. Med., Univ. Tehran, Iran). *Pharmacology*
9(6):374-376, 1973.

ᴬspirin (200 mg/kg, p.o.) caused gastric mucosal ulceration in each of 10 rats (100%) to whom it was administered. Pretreatment of the rats with α-methyldopa (12.5, 25, and 50 mg/kg, i.p.) reduced the percentage of rats with ulcers to 80%, 60%, and 20%, resp. Pretreatment with disulfiram (100, 200, and 400 mg/kg, i.p.) reduced the percentage of rats with ulcers to 50%, 30%, and 20, resp. It is suggested that the sympathetic nervous system may be important in the pathogenesis of aspirin-induced gastric ulceration in rats.

403 GASTRIC ACID SECRETION IN DIFFERENT STRAINS OF RATS DURING PYLORIC LIGATION
ND CHOLINERGIC STIMULATION. *(E.)* Vagne, M.;
argier, M. C.; Desvigne, A.; Daniere, S.; Lambert,
. (Edward Herriot Hosp., Lyon, France). *Digestion*
(4):308-316, 1973.

astric acid secretion was studied in 4 strains of
ats paired by age during a 3-hr pyloric ligation.
he rats were injected with carbaminoylcholine
25-200 μg/kg). In all strains, carbaminoylcholine
aused significant increases in gastric acid output
n direct relation to increasing doses of the stimu-
ant up to 50 μg/kg. The increase in gastric acid
ecretion decreased from Sherman to Sprague-Dawley,
ong-Evans, and Wistar. The fact that the difference
ersists during a maximal cholinergic stimulation
upports the hypothesis that it might be related to a
ariation in parietal cell mass or to a difference
f vagal tone. A direct comparison of 3 groups of
erman and Wistar, paired by a weight from 130-200
, eliminates the possibility that this variation
mong strains is due to difference in weight.
erefore, the strain is a determinant factor for
astric response to carbaminoylcholine.

404 STUDY OF THE VALUE OF BLACKMAN'S TABLES FOR NORMAL GASTRIC SECRETION: USE OF
R RESULTS FOR NORMAL SUBJECTS AND PATIENTS WITH
ODENAL ULCER. *(Sp.)* Rodrigo Gomez, J. M.;
arisi Quereda, L.; Serra Desfilis, M. A.; Guix
rcia, J.; Bixquert Jimenez, M.; Tomas Ridocci,
M.; Parrilla Paricio, P.; Montes Suay, F. (Fac.
ed., Valencia, Spain). *Rev. Esp. Enferm. Apar.*
g. 40(4):341-354, 1973.

05 THE LAI EXPERIMENTAL MODEL IN THE PHARMACOLOGICAL STUDY OF GASTRIC SECRETION AFTER
MINISTRATION OF VARIOUS STIMULANTS. *(Sp.)* Sanchez
la Cuesta, F.; Monfort Albelda, R.; Aznar Lopez,
(Inst. Gen. Ther., Univ. Sevilla, Spain). *Rev.*
p. Enferm. Apar. Dig. 38(7):795-802, 1972.

6406 THE CHYMOSIN ACTIVITY OF THE GASTRIC AND DUODENAL JUICE PROTEINASES SEPARATED BY MEANS OF AGAR GEL ELECTROPHORESIS. *(Ger.)* Kamaryt, J.; Mechlova, V. (Pediatric Inst., Bron, Czechoslovakia). *Z. Klin. Chem. Klin. Biochem.* 11(9):398-402, 1973.

6407 RESECTION OF THE LIVER AND THE SECRETORY FUNCTION OF THE STOMACH. *(Rus.)* Izraelashvili, M. S.; Toidze, O. S.; Tsertsvadze, T. N. (no affil.). *Soobsch. Akad. Nauk Gruz. SSSR* 69(3):677-680, 1973.

6408 HISTOCHEMICAL STUDY OF THE SECRETORY ACTIVITY OF THE GASTRIC MUCOSA IN DOGS. *(Fr.)* Gerard, A. (Univ. St. Pierre, Hosp., Brussels, Belgium). *Ann. Anat. Pathol. (Paris)* 17(3):355-378, 1972.

6409 EXPERIMENTAL CONTRIBUTION TO THE PHARMACOLOGICAL PATHOPHYSIOLOGY OF GASTRIC ACID AND PEPSIN SECRETION. *(Sp.)* Sanchez de la Cuesta y de Alarcon, F. (Fac. Med., Sevilla, Spain). *Rev. Esp. Enferm. Apar. Dig.* (suppl.):1-78, 1973.

6410 THE RADIOIMMUNOASSAY OF GASTRIN. *(E.)* Kaess, H. (Med. Clin. Univ. Heidelberg, Germany). *Acta Hepatogastroenterol.* 20(1):1-5, 1973.

6411 TEMPERATURE CHANGES AFTER SECRETORY RESPONSE IN THE PARIETAL AND NON-PARIETAL REGION OF THE NORMAL, VAGOTOMIZED AND PARTIAL RESECTED CANINE STOMACH. *(E.)* Kazil, P.; Klopper, P. J. (Lab. Exp. Surg., Univ. Amsterdam, Netherlands). *Acta Hepatogastroenterol.* 20(3):235-241, 1973.

6412 THE EFFECT OF COMMERCIAL CHOLECYSTOKININ (CCK-PZ) ON ACID AND PEPSIN SECRETION IN MAN. *(E.)* Petersen, H.; Berstad, A. (Ullevaal Univ. Hosp., Oslo, Norway). *Acta Hepatogastroenterol.* 20:330-337, 1973.

6413 ULCERATIVE EFFECT OF THE ADRENAL CORTEX AND 1,2-DEHYDROCORTISONE IMPLANTED INTO THE STOMACH WALL IN A RABBIT (HISTOCHEMICAL INVESTIGATION). *(Rus.)* Grenda, I.; Musyal, V.; Nivelinski, I.; Sokolovska-Pitukhova, Y.; Zamorska, L. (Med. Acad., Krakow, Poland). *Arkh. Patol.* 34(10):29-35, 1972.

6414 STUDY ON INHIBITION OF GASTRIC JUICE SECRETION IN MAN BY THE ATROPINE DERIVATIVE N-ISOPROPYLNORTROPINE-TROPA-ACID-ESTER-BROMOMETHYLATE. *(Ger.)* Otto, P. (Hannover Med. Coll., Germany). *Arzneim. Forsch.* 23(9): 1334-1336, 1973.

6415 EFFECT OF SMOKING ON GASTRIC ACID SECRETION *(E.)* Fung, W. P.; Tye, C. Y. (Fac. Med., Univ. Singapore). *Aust. N.Z. J. Med.* 3(3):251-254, 1973.

6416 DETERMINATION OF RENNIN AND PEPSIN IN BOVINE GASTRIC JUICE. *(Fr.)* Antonini, J.; Cisneros, F. (Lab. Biochem. Milk, Natl. Ctr. Sci. Invest., Havana, Cuba). *Biochimie* 55(2):221-226, 1973.

6417 THE ANTRAL CONTROL OF GASTRIC SECRETION. *(E.)* Monetti, G. (no affil.). *Chir. Gastroenterol.* 7(2):191-229, 1973.

6418 STUDY OF GASTRIC pH AND VARIATIONS AFTER ABSORPTION OF SODIUM BICARBONATE IN FASTING BEAGLE DOG. *(Fr.)* Labrid, C.; Duchene Marullaz, P.; Dureng, G.; Baissat, J. (Lab. Pharmacodynamics, C. E. R. M., Riom, France). *J. Physiol. (Paris)* 66(1):31-42, 1973.

6419 TECHNIQUE FOR INVESTIGATING GASTRIC JUICE. *(Rus.)* Boger, M. M.; Dykul', N. M. (Inst. Physiol., Siberian Div. Acad. Sci. USSR, Novosibirsk). *Lab. Delo* (5):268-271, 1973.

6420 UNIFICATION OF LABORATORY METHODS FOR STUDYING GASTRIC SECRETORY FUNCTION. *(Rus.)* Tugolukov, V. N. (no affil.). *Lab. Delo* (5):271-273, 1973.

6421 A QUANTITATIVE STUDY OF THE EFFECTS OF ANAESTHESIA AND STRESS OF OPERATION ON GASTRIC SECRETION IN RATS. *(E.)* Dai, S.; Ogle, C. W. (Fac. Med., Univ. Hong Kong). *Life Sci.* 13(4):327-333, 1973.

6422 CHANGES IN THE PROTEOLYTIC ACTIVITY OF GASTRIC JUICE IN EXPERIMENTAL ULCERS IN DOGS. *(Rus.)* Amirov, N. Sh.; Fernandez-Costa, J. (Inst. Normal Pathol. Physiol., Moscow, USSR). *Patol. Fiziol. Eksp. Ter.* (2):80-83, 1973.

6423 EFFECT OF 898 CERM ON HUMAN GASTRIC MUCOSA. *(Fr.)* Paris, J.; Delmotte, J. S.; Filoche, B. (Univ. Hosp. Ctr., Lille, France) *Rev. Fr. Gastroenterol.* (85):59-64, 1973.

See also, 6352, 6440, 6676, 6692, 6922, 7051, 7111, 7130. 7151, 7196.

SECRETION AND METABOLISM

Pancreas

6424 THE PHASES OF PANCREATIC SECRETION IN RATS. *(E.)* Shaw, H. M.; Heath, T. J. (Sch. Physiol. Pharmacol., Univ. New South Wales, Kensington, Australia). *Q. J. Exp. Physiol.* 58(3):229-237, 1973.

The flow of pancreatic juice and the bicarbonate and protein outputs decreased in conscious male albino rats with biliary and pancreatic duct cannulae during infusion of xylocaine (1.8 mg/hr), reaching values 22-44% lower than those recorded in control periods. Shortly after these same 14 rats were allowed access to 3 g of food; the flow of pancreatic juice and its output of bicarbonate and protein increased significantly. Similar increases in pancreatic secretion occurred when the rats had food injected directly into the intestine. When agar was similarly infused into the intestine to cause distension, an increase of 18-27% of the total pancreatic response to food injected directly into the intestine occurred. All these responses were greatly reduced by intraduodenal infusion of a local anesthetic during normal feeding. This seems consistent with the hypothesis that the intestinal phase of pancreatic secretion in rats, to which distension effects may contribute, may be responsible for the major part of the pancreatic response to feeding, and that in contrast to the situation in other mammals, the cephalic and gastric phases are of minor importance.

6425 ISOLATED DOG PANCREAS PLACED UNDER EXTRACORPOREAL CIRCULATION. STUDY OF ENZYME SECRETION AFTER INJECTION OF LABELED LEUCINE. *(Fr.)*

Laval, J.; Frexinos, J.; Laval, J. P.; Serres, P.; Lenet, R.; Martinel, C.; Ribet, A. (Purpan Hosp., Toulouse, France). *C. R. Soc. Biol. (Paris)* 167(1):141-147, 1973.

Isolated dog pancreas was perfused with fresh heparinized whole blood, glucose (0.60 g/hr), and sodium bicarbonate (3 mEq/hr). Five min after injection of secretin (10 or 20 clinical U/hr), the volume of pancreatic juice increased until a plateau was reached after 20 min when the rate of secretion stabilized at 0.5 ml/min. After 3-3.5 hr the rate of secretion decreased again. The total protein concentration of pancreatic juice averaged 1-2 mg/ml, while lipase activities averaged 200 IU/ml and amylase activities averaged 2000 IU/ml. Leucine, labeled with ^{14}C or ^{3}H, disappeared rapidly from the blood and was found, after a latent period of 20-25 min, in the trichloroacetic acid-insoluble fraction of pancreatic juice where it continued to be secreted for 25-30 min. The radioactivity of pancreatic juice increased linearly with time, but the rate of its increase was proportional to the dose of secretin used.

6426 REGENERATION OF THE PANCREAS IN THE RAT: FUNCTIONAL AND MORPHOLOGICAL FEATURES AFTER ALLOXAN OR ETHIONINE ADMINISTRATION AND AFTER PARTIAL RESECTION. *(Fr.)*

Ottolenghi, A.; Chiamenti, C.; Bosello, O.; Bettili, G. (Inst. Spec. Surg. Pathol. Clin. Propedeutics, Univ. Padua, Italy). *Nouv. Presse Med.* 2(3):153-157, 1973.

Pancreatic exocrine function and regeneration were studied in 4 groups of young rats: (1) 20 were subjected to right pancreatectomy (60%) and splenectomy; (2) 36 received moderate doses of ethionine (75 mg/kg/day i.p. for 10 days), 20 of which were then subjected to left pancreatectomy; (3) 50 rats received alloxan (80 mg/kg i.v.) followed by decreasing doses of insulin for 20-30 days; and (4) 20 rats which survived alloxan injection were subjected to partial pancreatectomy after 3-4 days. Pan- reatic morphology, amylase activity, and secretion fter stimulation with secretin and pancreozymin ere compared with values obtained for 12 controls. n all 4 groups of rats amylase activities and re- ponses to secretin and pancreozymin stimulation ere initially reduced and gradually returned to values approaching normal after 60-90 days. Degenerative changes in the pancreas, observed immediately after surgery, were followed by rapid regeneration which came to an end after 60 days. Both morphological and functional changes were most pronounced in group (4). These findings suggest that regenerated cells are not yet functionally mature at the end of 90 days in pancreatectomized, alloxan-treated rats.

6427 PANCREATIC EXOCRINE RESPONSES TO TEST MEALS OF VARYING COMPOSITIONS IN MAN. *(E.)* 6427

Lurie, B.; Novis, B. H.; Brom, B.; Bank, S.; Marks, I. N. (Groote Schuur Hosp., Cape Town, South Africa). *Am. J. Dig. Dis.* 18(10):847-850, 1973.

Test meals containing different proportions of fat, protein, carbohydrate, water, or sodium chloride were given to 9 subjects with no history of abdominal symptoms or heavy alcohol intake to study exocrine pancreatic secretion. A total of 34 test meals were used. Volume measurements were of no significance in the different test meals as there were marked fluctuations. The pH of duodenal aspirate remained fairly constant throughout the test. There were no significant differences between the pancreatic amylase, trypsin, and lipase concentrations following the various test meals. Thus, it is suggested that different types of food given orally stimulate exocrine pancreatic secretion in a similar way. The results confirm previous reports that there is no adaptive response of pancreatic enzymes to a single administration of different types of food.

6428 PARALLEL SECRETION OF CALCIUM AND ENZYMES BY THE HUMAN PANCREAS. *(E.)*

Goebell, H.; Baltzer, G.; Schlott, K. A.; Bode, C. (Med. Clin., Univ. Marburg, Germany). *Digestion* 8(4): 336-346, 1973.

Secretion of calcium, bicarbonate, and 4 pancreatic hydrolases into the duodenal juice was studied in groups of normal subjects (14 males and 4 females; aged 30-74 yr); patients with cholecystectomy (2 males and 7 females; aged 32-62 yr), relapsing chronic pancreatitis (5 males and 5 females; aged 20-63 yr). The pancreas was stimulated by a constant infusion of secretin (1 U/kg/hr) which resulted in a plateau of secretion after about 30 min. An injection of pancreozymin (1 U/kg) followed after 60 min and produced a significant increase in concentration and output of both calcium and enzymes. Both parameters were positively correlated. In cases with cholecystectomy, pancreozymin produced a similar parallel increase of secretion of calcium and enzymes. Since the influx of the bile into the duodenum was not changed, the amount of calcium stimulated by pancreozymin in the pancreas could be calculated at 5.2 μEq/min. In the group with pancreatic insufficiency, pancreozymin failed to evoke any increased secretion of calcium and enzymes. The results indicate that calcium enters human pancreatic juice in close association with pancreatic enzyme protein, having originated in the acinar cell, and that this process is governed by pancreozymin-cholecystokinin.

6429 THE CEPHALIC [PSYCHIC AND SENSORIAL] PHASE OF PANCREATIC SECRETION OBTAINED BY INTUBATION OF THE PANCREATIC DUCT IN MAN. *(It.)* Fontana, G.; Gullo, L.; Tessari, R. (1st Inst. Special Med. Pathol. Clin. Methodol., Univ. Bologna, Italy). *G. Clin. Med.* 52(12):855-874, 1971.

Cholecystectomy, followed by papillosphincterotomy and duodenostomy, was performed on 4 patients with gallstones. A thin, polyvinyl catheter was placed inside a triple-lumen tube, and the distal end of the catheter was introduced into the pancreatic duct; the other 2 lumina were used to aspirate the gastric and duodenal contents. Experiments were performed on patients at complete rest 2-3 days after surgery. Talking to patients about their favorite foods caused a significant increase in the volume of pancreatic secretion and in the bicarbonate and protein concentration and output after 10-20 min. Showing patients their favorite foods increased the volume of pancreatic secretion significantly after 10-40 min, the bicarbonate concentration after 10-20 min, the bicarbonate output after 10-50 min, and the protein concentration and output after 20-30 min. Sham feeding caused a significant increase in the volume of pancreatic secretion after 20-40 min, in the bicarbonate concentration after 20 min, in bicarbonate output after 10-40 min, in the protein concentration after 10-40 min, and in the protein output after 20-60 min. Administration of a parasympatholytic agent, isopropamide (4.5 mg parenterally), inhibited or greatly reduced responses to all 3 forms of stimulation, suggesting that psychic and sensorial stimulation of pancreatic secretion is mediated by the vagus nerve.

6430 EFFECTS OF CIGARETTE SMOKING ON BICARBONATE AND VOLUME OF DUODENAL CONTENTS. *(E.)* Bochenek, W. J.; Koronczewski, R. (Acad. Med., Wroclaw, Poland). *Am. J. Dig. Dis.* 18(9):729-733, 1973.

The effect of smoking on bicarbonate and volume of duodenal juice was studied in 25 male patients (aged 18-70 yr). Diagnoses included duodenal ulcer (8), gastric ulcer (2), irritable bowel syndrome (11), and rheumatic heart disease (4). It was found that in the basal condition smoking produced immediate and steady decreases in bicarbonate content and volume of duodenal samples. On the contrary, during pancreatic stimulation with secretin at approximately 50% of maximal secretion, smoking resulted in significant increases in bicarbonate output and volume. This stimulation arises partly from the vagolytic effect of nicotine resulting from competition between nicotine and acetylcholine for a cholinergic receptor. Decrease in buffering power of duodenal juice in the basal condition might explain why the most harmful effects of smoking in peptic ulcer patients occur in the fasting state.

6431 INTRALUMINAL AND POSTABSORPTIVE EFFECTS OF AMINO ACIDS ON PANCREATIC ENZYME SECRETION. *(E.)* DiMagno, E. P.; Go, V. L. W.; Summerskill, W. H. J. (Mayo Clin., Rochester, N.Y.). *J. Lab. Clin. Med.* 82(2):241-248, 1973.

In 38 healthy male volunteers (aged 21-56 yr), cholecystokinin-pancreozymin was measured by a bioassay method based on pancreatic enzyme output in response to essential amino acid perfusion of the small intestine. Essential amino acid perfusions of the duodenum, proximal jejunum, and distal jejunum evoked comparable trypsin outputs which exceeded basal secretion. In contrast, ileal perfusions yielded no increase over basal secretion. Therefore, cholecystoinin-pancreozymin is secreted throughout the human duodenum and jejunum, but not from the ileum. Simultaneous perfusions of essential amino acid at the duodenal and both jejunal sites evoked less trypsin output than at any 1 of these sites and was accompanied by increases of plasma glucagon and alpha-amino nitrogen. Similar inhibition of the effect of endogenous cholecystokinin-pancreozymin on the pancreas was caused by i.v. protein hydrolysate and was accompanied by increases of plasma glucagon. Glucagon, i.v., also inhibited the stimulatory effect of endogenous cholecystokinin-pancreozymin on pancreatic enzyme output. It is proposed that products of protein digestion in the small intestine stimulate pancreatic enzyme secretion by liberating cholecystokinin-pancreozymin and, after absorption, decrease pancreatic secretion probably by causing glucagon release.

6432 THE EFFECT OF THE β-RECEPTOR BLOCKADE (PROPRANOLOL) ON THE ENDOCRINE AND EXOCRINE PANCREATIC FUNCTION IN MAN AFTER THE ADMINISTRATION OF INTESTINAL HORMONES (SECRETIN AND CHOLECYSTOKININ-PANCREOZYMIN). *(E.)* Raptis, S.; Dollinger, H.; Chrissiku, M.; Rothenbuchner, G.; Pfeiffer, E. F. (Ctr. Intern. Med. Pediatr., Univ. Ulm, Germany). *Eur. J. Clin. Invest.* 3(3):163-168, 1973.

The effect of propranolol (3 mg, i.v., for 5 min, followed by 7 mg, continuous infusion, 75 min) on the induction of endocrine and exocrine pancreatic function by secretin and cholecystokinin-pancreozymin was investigated in 35 metabolically normal subjects (20-30 yr of age). Insulin secretion induced by i.v. glucose or secretin was significantly inhibited by propranolol. Under the influence of propranolol, the maximum glucose-induced serum insulin value dropped from 78 to 28 μU/ml and the maximum secretin-induced insulin value from 75 to 41 μU/ml. In contrast, propranolol did not inhibit insulin secretion induced by cholecystokinin-pancreozymin, the peak serum insulin value of 45 μU/ml remaining unchanged after propranolol infusion. The rise in insulin caused by secretin, cholecystokinin-pancreozymin, and glucose was associated with a significant fall in serum free fatty acids; this fall was further increased by propranolol administration. Exocrine pancreatic function was not influenced by propranolol. These results suggest that the action of secretin on the islet system, like that of glucose, is linked to the β-andrenergic system.

6433 EFFECTS OF A BETA-ADRENERGIC RECEPTOR STIMULANT (ISOPROTERENOL) ON PANCREATIC EXOCRINE SECRETION. *(E.)* Rudick, J.; Gonda, M.; Rosenberg, I. R.; Chapman, M. L.; Dreiling, D. A.; Janowitz, H. D. (Mt. Sinai Sch. Med., New York, N.Y.). *Surgery* 74(3):338-343, 1973.

The effects of isoproterenol on pancreatic secretion was studied in 5 dogs with chronic pancreatic and gastric fistulas. Pancreatic secretion was stimulated by secretin (0.03 U/kg/min) or secretin with cholecystokinin-pancreozymin (0.05 U/kg/min) infusion. Isoproterenol (0.25-2.0 μg/kg/min, i.v.) was administered during steady state secretion. Marked inhibition of volume, bicarbonate concentration, and bicarbonate output occurred. The degree of inhibition was dose related (30% at 0.25 μg/kg/min and 90% at 2.0 μg/kg/min). Enzyme responses to secretin with cholecystokinin-pancreozymin were profoundly inhibited by all doses of isoproterenol equally. The effective dose producing 5% inhibition was 0.6 μg/kg/min for bicarbonate output and < 0.25 μg/kg/min for enzyme output. These effects could be blocked by propanolol. Thus, isoproterenol, in doses which increase splanchnic blood flow, is an effective inhibitor of pancreatic electrolyte and enzyme secretion. This characteristic, coupled with its cardiovascular effects, suggests it may be valuable in the management of severe acute pancreatitis.

6434 EFFECT OF ETHANOL ON PANCREATIC AND BILIARY SECRETIONS IN HUMANS. *(E.)* Marin, G. A.; Ward, N. L.; Fischer, R. (Philadelphia Gen. Hosp., Pa.). *Am. J. Dig. Dis.* 18(10): 825-833, 1973.

The effect of various doses of ethanol on pancreatic and biliary secretions was studied in 7 normal subjects (6 males and 1 female, aged 21-37 yr) and in 3 patients (aged 24-40 yr) with alcoholic pancreatitis. Duodenal aspirate composition after ethanol administration was compared with that obtained after isotonic saline administration. A multilumen tube was used to perfuse a nonabsorbable marker (phenol red) into the duodenum, to collect duodenal secretions, and to perfuse saline or ethanol 45 cm beyond the ligament of Treitz. After the equilibration period, 3 20-min basal collections were obtained. After ethanol was started, 9 more collections were made. Jejunal perfusion of isotonic (1.39%) alcohol, at rates at which no significant blood ethanol levels could be detected, did not change pancreatic or biliary secretions in either group. On the other hand, jejunal or i.v. alcohol administration in doses of 1 g/kg markedly reduced the volume and outputs of pancreatic enzymes, bicarbonate, and bile salts. The decrease in outputs was accompanied by a corresponding diminution in concentrations. Therefore, acute administration of large doses of ethanol causes rapid changes in the composition of duodenal aspirates in humans. These changes cannot be totally explained by postulating a spasm of the sphincter of Oddi.

6435 PENTAGASTRIN AND SECRETIN AS EXTERNAL PANCREATIC SECRETAGOGUES IN MAN. *(Sp.)* Brasca, A. P.; Casabuena, B.; Laudano, O.; Gomez, R.; Cortes, J. (Natl. Centenary Hosp., Fac. Med., Rosario, Argentina). *Acta Gastroenterol. Latinoam.* 4(4):143-146, 1972.

6436 PROTEINS IN HUMAN PANCREATIC JUICE. *(Fr.)* Figarella, C. (Res. Unit Dig. Dis., I.N.S.E.R.M., Marseille, France). *Arch. Fr. Mal. App. Dig.* 62(4):337-353, 1973.

6437 TRYPSIN-PANCREATIC SECRETORY INHIBITOR (KAZAL INHIBITOR) INTERACTION. KINETIC AND THERMODYNAMIC PROPERTIES. *(E.)* Schweitz, H.; Vincent, J. P.; Lazdunski, M. (Ctr. Biochem., Univ. Nice, France). *Biochemistry* 12(15):2841-2846, 1973. 2841-2846, 1973.

6438 PHOSPHOLIPASE A ACTIVITY OF HUMAN DUODENAL FLUID. *(Fr.)* Thouvenot, J. P.; Durand, S.; Douste Blazy, L. (Lipid Biochem. Unit., INSERM, Purpan, France). *Clin. Chim. Acta* 44(3):391-397, 1973.

6439 LIPOMATOSIS OF THE EXOCRINE PANCREAS AFTER D-PENICILLAMINE FEEDING IN RATS ON A CHOLINE-DEFICIENT DIET. *(Ger.)* Perings, E.; Brunner, G.; Bokermann, M.; Track, N. S.; Schmidt, H.; Creutzfeldt, W. (Med. Clin., Univ. Gottingen, Germany). *Dtsch. Med. Wochenschr.* 98(21):1085-1086, 1973.

6440 LYMPHATICS: THE TRANSPORT ROUTE FOR INTERNAL SECRETION OF ENZYMES BY GASTROINTESTINAL GLANDS. *(Rus.)* Korot'ko, G. F.; Batkaeva, N. Kh. (M. I. Kalinin State Med. Inst., Andizhan, USSR). *Fiziol. Zh. SSSR* 59(6):924-930, 1973.

6441 THE PERMEABILITY KINETICS OF THE HISTOHEMATIC BARRIERS IN CHRONIC ACTION OF CCl_4. *(Rus.)* Yudina, T. V.; Novikov, Y. V. (F. F. Erisman Res. Inst. Hyg., Moscow, USSR). *Gig. Sanit.* (2):29-34, 1973.

6442 THE INFLUENCE OF PANCREAS RESECTION ON THE FUNCTION AND MORPHOLOGY OF SOME INTERNAL ORGANS. *(Rus.)* Pipia, E. K.; Gabisonia, G. T. (no affil.). *Soobsch. Akad. Nauk, Gruz. SSSR* 70(3): 737-740, 1973.

6443 THE EFFECT OF DRY BREWER'S YEAST ON THE EXTERNAL SECRETORY FUNCTION OF THE PANCREAS. *(Rus.)* Vorobieva, T. V. (Inst. Nutrition, Moscow, USSR). *Vopr. Pitan.* (2):44-46, 1973. 1973.

6444 GLUCAGON AND ITS IMPORTANCE FOR REGULATION OF EXOCRINE PANCREATIC FUNCTION. *(Ger.)* Schulz, H. J.; Dietze, F.; Schliack, V. (1st Med. Clin., Humboldt Univ., Berlin, Germany). *Z. Gesamte Inn. Med.* 28(11):313-320, 1973.

6445 EFFECT OF ENDOGENOUS AND EXOGENOUS GASTRIN ON THE SECRETION OF INSULIN IN MAN. *(E.)* Rehfield, J. F.; Stadil, F. (Bispebjerg Hosp., Copenhagen, Denmark). *Israel J. Med. Sci.* 8(6): 761-763, 1972.

6446 EFFECT OF ELECTRICAL STIMULATION OF THE GASTROINTESTINAL TRACT ON PANCREATIC ENZYME ACTIVITY IN PATIENTS WITH TRAUMATIC SPINAL CORD INJURIES. *(Rus.)* Vishnevskii, A. A.; Livshits, A. V.; Khrushcheva, E. A.; Karvonidi, P. G.; Kolpachkov, V. A. (A. V. Vishnevskii Inst. Surg., Moscow, USSR). *Kazan. Med. Zh.* (3):1-6, 1973.

6447 MEASUREMENT OF THE BIOLOGICAL ACTIVITY OF SYNTHETIC SECRETIN. *(Ger.)* Lehnert, P.; Stahlheber, H.; Roder, O.; Zoelch, M.; Forell, M. M.; Wunsch, E.; Jaeger, E.; Martens, H. L. (2nd Med. Clin., Univ. Munich, Germany). *Klin. Wochenschr.* 51(1):44-46, 1973.

6448 PANCREATIC SECRETION IN MAN AFTER STIMULATION WITH CHOLECYSTOKININ/PANCREOZYMIN, SECRETIN AND BILE. METHODS AND NORMAL RANGES. *(E.)* Otte, M.; Stahlheber, H.; Zoelch, M.; Forell, M. M. (2nd Med. Clin., Univ., Munich, Germany). *Klin. Wochenschr.* 51(18):915-920, 1973. 1973.

6449 PANCREATIC RIBONUCLEASE DISTRIBUTION AND COMPARISONS IN MAMMALS. *(E.)* Beintema, J. J.; Scheffer, A. J.; Van Duk, H.; Welling, G. W.; Zwiers, H. (Biochem. Lab., Natl. Univ., Groningen, Netherlands). *Nature* [*New Biol.*] 241(107):76-78, 1973.

See also, 6132, 6214, 6372, 6389, 6401, 7178, 7520.

SECRETION AND METABOLISM

Hepatobiliary Tract

6450 EXPERIMENTAL HEPATIC NECROSIS: STUDIES ON COAGULATION ABNORMALITIES, PLASMA CLEARANCE, AND ORGAN DISTRIBUTION OF ^{125}I-LABELLED FIBRINOGEN. *(E.)* Rake, M. O.; Flute, P. T.; Pannell, G.; Shilkin, K. B.; Williams, R. (King's Coll. Hosp., London, England). *Gut* 14(7):574-580, 1973.

In female virgin rats given carbon tetrachloride (CCl_4), hepatic necrosis was evident by 7 hr and maximal at 28-35 hr. Macroscopic bleeding was not evident. The mean prothrombin time was no different from controls in carbon tetrachloride-dosed animals at 7 hr. However, the prothrombin time had increased to 19.9 sec. at 14 hr after dosing and to 25.8 sec at 21 hr. At 35 hr the mean value was 65 sec, compared with 32 sec for controls. There was no reduction in the plasma fibrinogen level. Heparin 450 U/kg, i.p.) was given to 5 rats. Tranexamic acid (0.1 g/kg, i.p.) was given to another 5. Both drugs were given to 5 additional rats. Macroscopic bleeding was observed in about 1/4 of the animals receiving heparin. The increased rate of removal of ^{125}I fibrinogen from the plasma in animals with CCl_4-induced hepatic necrosis was further increased by tranexamic acid and decreased to some extent by heparin, although not to control values. In animals receiving heparin, the onset of hepatic necrosis was delayed to 14 hr and did not maximize until 35 hr. Tranexamic acid speeded the appearance of hepatic necrosis which was maximum at 21 hr. Tranexamic acid delayed accumulation of radioactivity in liver and spleen. Excess radioactivity was found in the kidney. These results confirm that acute hepatic necrosis is associated with increased utilization of fibrinogen which may intensify the hemostatic defect and, because of the deposition of intravascular fibrin, may be responsible for further ischemic necrosis to the tissues. Although heparin administration may reduce the loss of fibrinogen, interference with a normal compensating mechanism of fibrinolysis is clearly contraindicated.

6451 HEPATOTOXICITY OF 5-AZACYTIDINE (A CLINICAL AND PATHOLOGIC STUDY). *(E.)* Bellet, R. E.; Mastrangelo, M. J.; Engstrom, P. F.; Custer, R. P. (American Oncol. Hosp., Philadelphia, Pa.). *Neoplasma* 20(3):303-309, 1973.

5-Azacytidine (0.80-2.20 mg/kg/day, s.c., for 10 successive days) was administered to 25 patients (11 men and 14 women, aged 32-77 yr) with a variety of advanced malignant tumors. Of 20 patients who could be evaluated for drug toxicity, 7 had abnormal liver function and 4 with large liver tumors died of rapidly progressive hepatic coma. A comparison of survivors with hepatic metastases and those dying of hepatic coma revealed that patients who died had baseline serum albumins of less than 2.8 g/100 ml while survivors had values of more than 3.0 g/100 ml. It is concluded that 5-azacytidine is contraindicated in patients with hepatic metastases and serum albumin concentrations lower than 3.0 g/100 ml, even though serum bilirubin and prothrombin times may be normal and SGOT and alkaline phosphatase activities only slightly elevated. Histological evaluation of percutaneous needle biopsies of the liver in 8 patients (3 men and 5 women, aged 33-7 yr) with extrahepatic tumors and no evidence of hepatic metastases showed no significant differences between specimens obtained before and after 5-azacytidine therapy.

6452 INCREASE OF MICROSOMAL GLUCOSE-6-PHOSPHATASE ACTIVITY AFTER CHRONIC ETHANOL ADMINISTRATION. *(E.)* Ishii, H.; Joly, J. G.; Lieber, C. S. (Mt. Sinai Sch. Med., New York, N.Y.). *Metabolism* 22(6):799-806, 1973.

Female Sprague-Dawley rats were pair-fed liquid diets with 36% of total calories either as ethanol or isocaloric carbohydrate (controls). The remainder of the diet contained 35% of total calories as fat, 18% as protein, and 11% as additional carbohydrate. Ethanol feeding, as isocaloric substitution for carbohydrate, for a 6 week period significantly increased the activity of glucose-6-phosphatase both in fed (38%) and fasted (18%) rats when expressed per mg microsomal protein. When expressed per unit of body weight, the enzyme activity was increased 66% in fed and 43% in fasted rats. Another group of rats received diets containing 36% of calories as ethanol or isocaloric fat. The remainder of the diet contained 11% of total calories as carbohydrate, 18% as protein, and 35% as additional fat. This ethanol feeding as isocaloric substitution for fat over 6 weeks again increased glucose-6-phosphatase activity significantly. Ultracentrifugation in a Cs^+-containing sucrose gradient to separate rough and smooth microsomes revealed that the increase in glucose-6-phosphatase activity after ethanol feeding occurred mainly in the smooth microsomal membranes.

6453 THE EFFECTS OF ETHANOL ON HEPATIC LIPID PEROXIDATION AND ON THE ACTIVITIES OF GLUTATHIONE REDUCTASE AND PEROXIDASE. *(E.)* Macdonald, C. M. (Dept. Materia Med., Univ. Glasgow, Scotland). *F.E.B.S. Lett.* 35(2):227-230, 1973.

Male albino Sprague-Dawley rats were intubated with ethanol (5 g/kg/day for 1, 2, 5, or 10 weeks). After the livers had been removed, washed, and homogenized, mitochondria and microsomes were examined for diene conjugation, as a direct and sensitive method for measuring lipid peroxidation. Animals receiving ethanol for 1 week showed mitochondrial peroxidation but not microsomal peroxidation. In the 2-, 5-, and 10-week groups, there was peroxidation in both cellular compartments. Thus, it is concluded that the initial effect of ethanol is on the mitochondrial lipids, but, following chronic ethanol exposure, the effect becomes generalized. After livers from similarly treated rats were prepared, postmicrosomal supernatants were obtained and used to measure glutathione peroxidase and reductase enzyme activities. These activities increased about 45% and 15%, resp., which is consistent with an induction process. Thus, glutathione peroxidase may be an adaptable enzyme in a protective mechanism against lipid peroxide toxicity. The accompanying increase in the reductase probably results from the increased demand for gluthathione peroxidase. These results may help explain the ability to develop increased tolerance and catabolism of lipid peroxides.

6454 FATTY ACID COMPOSITION OF TISSUE LIPIDS IN CHOLINE DEFICIENT RATS. *(E.)* Chahl, J. S.; Kratzing, C. C. (Fac. Med., Univ. Papua New Guinea, Boroko). *Q. J. Exp. Physiol.* 58(3):275-284, 1973.

Male Wistar rats fed a choline-deficient diet for 3 weeks had up to 38% of their liver weight in lipids, compared with 6.5% in choline-supplemented controls. The mean value of liver triglycerides was 23 4 mg/g of lipid-free liver in the choline-supplemented group, and 500.9 mg/g in the choline-deficient group. Total liver phospholipid content did not change in choline deficiency, but the proportion of lecithin in phospholipids decreased from 47.32 to 38.3%. Thus, this large increase in liver lipids was due to triglyceride accumulation. Fatty acid composition was not altered in choline deficiency although the plasma triglyceride concentration of stearic acid was increased and that of oleic acid was decreased. In choline-deficient rats, the concentration of arachidonic acid was decreased in liver phospholipids while that of docosapolyenoic acids was increased. There were more widespread changes in the cholesterol ester fatty acids of liver and plasma in choline-deficient rats. It is proposed that selective impairment of transport of lipid species, depending on fatty acid composition, occurs in choline deficiency.

6455 THE EFFECT OF ANTRAL ACIDIFICATION ON BILE-INDUCED GASTRIC ACID SECRETION. *(E.)*

Nahrwold, D. L.; Rose, R. C.; Kaminski, D. L. (Pennsylvania State Univ., Coll. Med., Hershey). *Surgery* 74(3):315-320, 1973.

Acid secretion from canine Heidenhain pouches was monitored during perfusion of denervated, separated antral pouches with solutions of acetylcholine at a concentration known to produce maximal gastrin release, with 5 mM sodium glycocholate, and with canine hepatic whole bile having a 5.0 mM concentratraion of bile salt. The perfusates were adjusted to pH 7, 5, 3, 2, or 1. Results indicate that 5.0 mM bile salt is a potent stimulus when compared to other commonly used gastrin releasers and that bile and sodium glycocholate maintain their effectiveness as gastrin releasers at relatively low pH values. Reduction of pH from 3.0 to 2.0 resulted in a 57% decrease in acid secretion when acetylcholine was the perfusate, whereas the decrease was only 32% for sodium glycocholate and 35% for bile. The maximal gastric secretion in response to sodium glycocholate and to bile occurred at pH values known to exist in the resting stomach. These findings suggest that operations supposedly associated with increased reflux of bile into the antrum, such as pyloroplasty and gastrojejunostomy, with or without vagotomy, could be associated with significant gastric secretion through the release of gastrin by bile salts. It is further suggested that the presence of bile salts in the stomach at concentrations known to disrupt the gastric mucosal barrier could potentiate the mucosal injury through release of gastrin and increased acid secretion.

6456 HISTOAUTORADIOGRAPHIC STUDIES OF LIVER REGENERATION AFTER CCl_4 INTOXICATION.

(Ger.) Hubner, K.; Voigt, H. G. (Senckenberg Pathol. Inst., Johann Wolfgang Goethe Univ., Frankfurt/Main, Germany). *Med. Welt* 23(39):1345-1351, 1972.

A solution of carbon tetrachloride (0.0023 ml/g in olive oil) was injected i.p. into 30 white mice which were then anesthetized with ether and decapitated 3-326 hr later. ^{3}H-labeled thymidine was injected i.p. 2 hr before death, and DNA synthesis and mitosis were studied in the liver. This small dose of carbon tetrachloride caused rhythmic, rather than continuous, stimulation of DNA synthesis. The maxima for both DNA synthesis and mitosis occurred 2 and 8 days after administration of carbon tetrachloride; minima occurred after 24 hr and 6 days, resp. The maxima coincided with maxima in liver cell regeneration. DNA synthesis in Kupffer's cells decreased 3 hr after carbon tetrachloride injection and reached maxima after 3-4 days and after 8 days. The maxima for DNA synthesis in Kupffer's cells were much smaller than the maximum occurring in liver cells 6 days after injection of carbon tetrachloride. These findings confirm the results of previous studies on regeneration in the kidney which suggested that the first maximum results from parenchymal cell and the second from mesenchymal cell proliferation.

6457 STUDY OF h-PROTEINS IN THE LIVER OF ANIMALS WITH DIFFERENT SENSITIVITIES TO CARCINOGENS.

(Rus.) Kaledin, V. I. (Inst. Cytol. Genet., Novosibirsk, USSR). *Vopr. Onkol.* 18(6):57-60, 1972.

A protein fraction bound to 4-dimethylaminoazobenzene (DAB) was obtained from liver homogenates of adult Wistar rats which had been fed DAB (10 mg/day) for 2 weeks. The amino acid composition, sedimentation coefficient (3.75 S), and molecular weight (47,500) were identical to those of Sorof's h_2-protein. On immunoelectrophoresis this protein was separated into 2 fractions which differed in their motility in agar and their immunological specificity. The larger fraction, which had the greater electronegative motility, was called fraction h-A and the other fraction, h-B. Both of these protein fractions were nonspecific for the livers of species sensitive to carcinogenic azo dyes. By using antisera to these protein fractions, studies were made of the contents of h-protein in the livers and other organs of Wistar rats, *Sigmodon hispidis*, CC57Br and C3H mice, hamsters, guinea pigs, and chinchilla rabbits. h-Proteins were found in the livers of mice, which are sensitive to carcinogenic azo dyes, and in the livers of guinea pigs, hamsters, and *S. hispidis*, which are resistant to these carcinogens. The h-A fraction was detected in extracts from the kidneys and testes of rats, and the h-B fraction was found in rat testes, lungs, brain, and spleen and in the livers of newborn rats, which are resistant to DAB. However, h-proteins isolated from carcinogen-resistant species differed from the h-proteins of rat liver in their antigenic specificity and charge. h-Protein from the liver of *S. hispidis* did not bind DAB when this species was given the dye. Correlations were found between the h-protein content, particularly the content of the h-B fraction, of adult rat and mouse liver and the sensitivity of these animals to DAB and o-aminoazotoluene.

6458 THE METABOLISM OF 28 SERUM PROTEINS AFTER HUMAN LIVER TRANSPLANTATION. *(Ger.)* Muller, H. E.; Lie, T. S. (Inst. Med. Microbiol. Immunol., Univ. Bonn, Germany). *Z. Immunitaetsforsch.* 145(3):250-274, 1973.

During the entire 205-day survival period, quantitative determinations were made of 28 serum proteins, using one-dimensional immunodiffusion, in a 30-yr-old man who received a liver transplant for a hepatoma. The patient received immunosuppressives (prednisone, azathioprine, and horse antilymphocyte serum) during this entire period. Determinations made 7-35 days after surgery, when the patient was not being given blood transfusions, demonstrated that after latent periods varying in length the transplanted liver resumed synthesis of all 28 proteins investigated. No significant changes in protein metabolism were found during the first acute rejection reaction which occurred 6 days after surgery because (1) blood transfusions were still being given and (2) the rate of protein metabolism was slow at this time. The delayed rejection reaction, which occurred 110 days after surgery, was preceded by progressive decreases in some of the proteins and disturbances in liver function tests. Decreases in α_1-lipoprotein, haptoglobin, and Zn-α_2-glycoprotein, preceded progressive increases in serum direct and total bilirubin levels and SGOT, SGPT, and alkaline phosphatase activities. Decreases in the serum levels of these proteins may be a signal for liver rejection. Decreases in serum α_1-glycoprotein and prealbumin also occurred very early.

6459 ACID PRODUCTION IN THE ISOLATED PERFUSED RAT LIVER. *(E.)* Morland, J.; Christoffersen, T.; Osnes, J. B. (Inst. Pharmacol., Univ. Oslo, Norway). *Acta Physiol. Scand.* 89(1):61-67, 1973.

The release and production of organic acids were studied in isolated perfused livers from male albino Wistar rats. The livers were perfused at different pH (6.2-7.4) with and without ethanol. Liver homogenate pH was measured. The basal production of acid by the liver was greatest in the early phase of perfusion, probably due to the low initial concentration of acid metabolites in the perfusate. Acid production declined when perfusate pH was reduced and increased when perfusate pH was raised. Ethanol treatment (perfusate concentration 30-45 mM) increased liver acid production. Liver homogenate pH was more reduced when the H+ ion had an intracellular origin (i.e., after ethanol) than when H+ ions entered the perfusate outside the liver (i.e., after hydrochloric acid administration) at the same perfusate pH. Results obtained here allow the assumption that metabolically important increases in acidity occur in certain liver cell compartments after ethanol, accompanied by only slight alterations in whole liver homogenate and blood pH. If this is correct, pH-sensitive intracellular reactions could be influenced by ethanol metabolism at physiological pH values.

6460 RELEASE OF ENZYMES FROM A RAT LIVER LYSOSOME FRACTION: INHIBITION BY CATECHOLAMINES AND CYCLIC 3',5'-ADENOSINE MONOPHOSPHATE, STIMULATION BY CHOLINERGIC AGENTS AND CYCLIC 3',5'-GUANOSINE MONOPHOSPHATE. *(E.)* Ignarro, L. J.; Krassikoff, N.; Slywka, J. (CIBA-GEIGY Corp., Ardsley, N.Y.). *J. Pharmacol. Exp. Ther.* 186(1):86-99, 1973.

The *in vitro* release of enzymes from livers of male Sprague-Dawley rats was inhibited by adrenergic agents and cyclic 3',5'-adenosine monophosphate. This release was accelerated by cholinergic agents and cyclic 3',5'-guanosine monophosphate. Norepinephrine, epinephrine, and isoproterenol (10^{-4} M or higher) inhibited lysosomal enzyme release. Liver lysosome fractions contained adenyl cyclase and phosphodiesterase activities. Catecholamines stimulated adenyl cyclase activity, whereas propranolol, but not phentolamine, inhibited it. Theophylline, papaverine, and zinc chloride inhibited phosphodiesterase activity. Lysosomal enzyme release was accelerated by acetylcholine, acetyl-β-methylcholine, and carbamylcholine; this action was inhibited by atropine. Cyclic 3',5'-guanosine monophosphate accelerated lysosomal enzyme release and stimulated phosphodiesterase activity; atropine had no influence on either effect. Reduced *in vivo* levels of norepinephrine and epinephrine with reserpine (2.5 mg/kg/day for 3 days, s.c.) enhanced liver lysosome fragility, release of lysosomal enzymes, and elevated plasma levels of enzymes. In reserpine-treated rats, the repeated administration of 3,4-dihydroxyphenylalanine restored lysosome integrity. Catecholamine and cyclic 3',5'-adenosine monophosphate membrane-stabilizing action was more effective on lysosomes from reserpine-treated rats than from untreated controls. Enhanced liver lysosome fragility occurred in rats treated with 6-hydroxydopamine. These data suggest that the inflammatory process might be regulated by the autonomic nervous system by action of neurohormones and cyclic nucleotides on enzyme release from lysosomes.

6461 INHIBITION OF LIVER FIBROSIS BY L-AZETIDINE-2-CARBOXYLIC ACID IN RATS TREATED WITH CARBON TETRACHLORIDE. *(E.)* Rojkind, M. (Dept. Cell Biol., Res. Ctr., Advances Studies, IPN, Mexico D. F.). *J. Clin. Invest.* 52(10):2451-2456, 1973.

Hepatic cirrhosis was induced in male albino rats by carbon tetrachloride (0.15 ml in mineral oil, i.p., 3 times/week for 20 doses). L-Azetidine-2-carboxylic acid was administered in doses of 10 μmol, i.p., with each of the last 10 or with each of the 20 doses of carbon tetrachloride. In rats receiving 100 or 200 μmol of the drug, collagen synthesis dropped from a control value of 4.46 μmol/g to 1.93 and 1.55 μmol/g, resp., for proline and from 3.30 μmol/g to 0.88 and 0.61 μmol/g, resp., for hydroxyproline. Histological examination of liver specimens revealed that animals receiving L-azetidine-2-carboxylic acid had the same extent of liver necrosis and cellular regeneration as did control rats; however, the extent of fibrosis was greatly diminished. The synthesis of noncollagenous proteins in the livers of rats so treated was not affected. These results indicate that L-azetidine-2-carboxylic acid inhibits collagen synthesis and deposition in the cirrhotic liver.

6462 PROTECTION BY DIETHYLDITHIOCARBAMATE AGAINST CARBON TETRACHLORIDE LETHALITY IN RATS AND AGAINST CARBON TETRACHLORIDE-INDUCED LIPID PEROXIDATION IN VITRO. *(E.)* Lutz, L. M.; Glende, Jr., E. A.; Recknagel, R. O. (Sch. Med., Case Western Reserve Univ., Cleveland, Ohio). *Biochem. Pharmacol.* 22(14):1729-1734, 1973.

Male Sprague-Dawley rats received diethyldithiocarbamate (10-300 mg/kg, i.p.) 1 hr prior to carbon tetrachloride (5.0 ml/kg), which was administered by stomach tube. Doses of 100 and 300 mg/kg were 100% effective in protecting against carbon tetrachloride poisoning. Lower doses were less effective. Addition of 30 mM to 1.0 μM diethyldithiocarbamate to the incubation of liver microsome-supernatant fraction inhibited the peroxidation of constituent lipids as determined by the lack of production of malonic dialdehyde. Malonic dialdehyde production in a hepatic microsome-supernatant fraction supplemented with 0.2 mM reduced nicotinamide adenine dinucleotide phosphate and 0.3 mM glutathione was augmented by 1 μliter/ml carbon tetrachloride. Addition of diethyldithiocarbamate at 3 μM completely inhibited this pro-oxidant effect of carbon tetrachloride. Diethyldithiocarbamate has no inhibitory action on microsomal reduced nicotinamide adenine dinucleotide phosphate-cytochrome *c* reductase. These results suggest that inhibition of lipid peroxidation by diethyldithiocarbamate does not occur at the flavoprotein site, but elsewhere in the overall process of microsomal lipid peroxidation.

6463 THE RATE-LIMITING STEP IN THE BILIARY ELIMINATION OF SOME SUBSTRATES OF URIDINE DIPHOSPHATE GLUCURONYLTRANSFERASE IN THE RAT. *(E.)* Mulder, G. J. (Dept. Pharmacol., State Univ. Groningen, Netherlands). *Biochem. Pharmacol.* 22(14):1751-1763, 1973.

Phenolphthalein (0.075 mM), 4-methylumbelliferone (0.6 mM) and 8-hydroxychinoline (1.0 mM) mutually inhibit each other's enzymatic conjugation by microsomal uridine 5'-diphosphate glucuronyltransferase *in vitro*. After i.v. injection, these uridine 5'-diphosphate glucuronyltransferase substrates are excreted in the bile of male Wistar rats as β-D-glucuronides. When these glucuronides were injected i.v. they were excreted partially in the bile and also in the urine. Ligation of the kidneys caused increased biliary excretion of the i.v. injected glucuronides. To determine if these uridine 5'-diphosphate glucuronyltransferase substrates also inhibited each other's glucuronidation *in vivo*, 2 compounds were injected i.v. simultaneously into rats and the mutual effects on the biliary excretion of these compounds were studied. Phenolphthalein inhibited the biliary excretion of 4-methylumbelliferone in the form of its glucuronide conjugate in bile. This inhibition was not due to substrate competition for uridine 5'-diphosphate glucuronyltransferase but to inhibition of excretion of the formed glucuronides from the liver cell into bile. Further experiments on mutual inhibition of i.v. injected glucuronides in bile indicated that the rate-limiting step in the biliary elimination of phenolphthalein, 4-methylumbilliferone, and 8-hydroxychinoline as glucuronides in the rat is the excretion of the products of uridine 5'-diphosphate glucuronyltransferase activity *in vivo* into the lumen of the bile canaliculus, and not conversion by uridine 5'-diphosphate glucuronyltransferase.

6464 EFFECT OF AMINOTRIAZOLE ON ISOPROPANOL- AND ACETONE-INDUCED POTENTIATION OF CCl_4 HEPATOTOXICITY. *(E.)* Traiger, G. J.; Plaa, G. L. (Dept. Pharmacol., Univ. Montreal, Canada). *Can. J. Physiol. Pharmacol.* 51(4):291-296, 1973.

The effect of aminotriazole (1.0 g/kg, i.p.) on isopropanol- (2.5 ml/kg, p.o.) and acetone-induced (1.0 ml/kg, p.o.) potentiation of carbon tetrachloride (0.1 ml/kg, i.p.) hepatotoxicity, and on the *in vivo* metabolism of isopropanol and acetone was studied in male Sprague-Dawley rats. Aminotriazole plus isopropanol, 18 hr prior to a challenging dose of carbon tetrachloride, reduced the isopropanol-enhanced response of carbon tetrachloride SGPT activities were less than those found for isopropanol plus carbon tetrachloride. Hepatic triglyceride content also reflected reduced hepatotoxicity. Aminotriazole pretreatment did not change the rate of isopropanol elimination, nor was the rise and subsequent decline in the blood concentrations of the derived acetone altered. An 18 hr pretreatment with acetone enhanced carbon tetrachloride to acetone (reduced SGPT activities and hepatic triglyceride content). Aminotriozole had no effect on acetone elimination from the blood 1, 4, and 8 hr after the p.o. administration of acetone. Aniline hydroxylase activity was increased 17 hr after the administration of isopropanol. These results suggest that isoproparol augments carbon tetrachloride hepatotoxicity by affecting the microsomal drug-metabolizing enzyme system.

6465 FREE AND CONJUGATED BILE PIGMENTS OF BODY FLUIDS: QUALITATIVE ANALYSIS BY THIN-LAYER CHROMATOGRAPHY. *(E.)* Thompson, R. P. H.; Hofmann, A. F. (Mayo Clin., Rochester, Minn.). *J. Lab. Clin. Med.* 82(3):483-488, 1973.

The presence of bilirubin and its mono- and diconjugates in human and animal bile was studied by thin-layer chromatography. Normal human bile contains predominantly diconjugates. In 3 female patients with biliary obstruction an increased proportion of monoconjugates was observed, but in 1 of these the ratio of mono- and diconjugates reversed to normal after surgical treatment. The predominant pigment in bile from dog, cat, sheep, rat, pig, and ox had the mobility of a monoconjugate. Bile from the germfree rat was identical with that from the normal rat, indicating that bacterial deconjugation of the diconjugates in bile in this species cannot be responsible for the monoconjugate. Only free bilirubin was detected in human gallstones. Incubation of radiolabeled bilirubin diconjugate with β-glucuronidase demonstrated sequential liberation of bilirubin monoglucuronide and free bilirubin. It is suggested that conjugates, particularly monoconjugates, are originally precipitated in gallstones and then are slowly hydrolyzed *in situ* by β-glucuronidase in the bile.

6466 POST MORTEM CHARACTERISTICS OF THE HEPATIC MICROSOMAL DRUG OXIDISING ENZYME SYSTEM.

(E.) MacLeod, S. M.; Renton, K. W.; Eade, N. R. (Dept. Pharmacol., McGill Univ., Montreal. Canada). *Chem. Biol. Interact.* 7(1):29-37, 1973.

The stability of hepatic microsomal drug oxidation and its associated electron transport was studied in rabbits under conditions approximating those existing prior to human autopsy. Aminopyrine N-demethylation, aniline p-hydroxylation, reduced nicotinamide adenine dinucleotide phosphate (NADPH), cytochrome c reductase, NADPH cytochrome P-450 reductase, and the microsomal content of cytochrome P-450 declined appreciably in 2 hr when microsomes were prepared from rabbit liver left *in situ* after death. These microsomal components remained stable for at least 4.5 hr in livers removed immediately after death and kept on ice. Published data suggest that similar degeneration of microsomal activity takes place in human liver *post mortem.* The lability of hepatic microsomes from livers left *in situ* in these experiments or prior to autopsy is most likely secondary to slow cooling of the liver with coincidental autolysis. Bacterial cultures obtained from 6 livers left *in situ* for 0, 2, and 4.5 hr after death did not show growth of anaerobic or aerobic bacteria except for 1 case of a single zero time sample. Thus the possibility that the degeneration observed was due to the rapid growth of bacteria was disproved. These experiments demonstrate that care must be exercised in interpreting data obtained using microsomes from human autopsy material.

6467 STUDIES ON THE EFFECTIVENESS OF DIFFERENT METHODS FOR ENZYME INDUCTION IN MICE WITH PHENOBARBITAL.

(Ger.) Buzello, W.; Scholler, K. L.; Schoppe, B. (Inst. Anesthesiol., Univ. Freiburg/Breisgau, Germany). *Arzneim. Forsch.* 23(9):1337-1339, 1973.

A comparison was made of liver enzyme induction in female NMRI mice by administering phenobarbital i.p. or s.c. (100 mg/kg/day) or p.o. (0.01-1.0% in drinking water) for 5 days. After a 2-day interval the relative increase in liver weight and decrease in hexobarbital (100 mg/kg i.p.) sleeping time were determined for use as criteria in establishing the effectiveness of microsomal enzyme induction. The best results were obtained by administering 0.05% phenobarbital in the drinking water: hexobarbital sleeping time decreased by 45%, the relative liver weight increased to 5.8% of the body weight, body weight gain was not affected, and none of the mice died. Further studies demonstrated that the even better results can be obtained by administering 0.05% phenobarbital in the drinking water for 3 days and allowing a 24-hr interval before estimating enzyme induction. Mice treated in this way ingested an average of 140 ± 14 mg/kg/day of phenobarbital. The liver weight returned to normal within 2-3 days, and the hexobarbital sleeping time returned to normal within 4 days.

6468 REVERSIBILITY OF LIVER DAMAGE IN RATS RENDERED RESISTANT TO CARBON TETRACHLORIDE BY PRIOR CARBON TETRACHLORIDE ADMINISTRATION: BEARING ON THE LIPOPEROXIDATION HYPOTHESIS.

(E.) Ugazio, G.; Koch, R. R.; Recknagel, R. O. (Sch. Med., Case Western Reserve Univ., Cleveland, Ohio). *Exp. Mol. Pathol.* 18:291-289, 1973.

Male Sprague-Dawley rats were given carbon tetrachloride (25 microliter/100 gm of body weight in mineral oil, intragastrically) over a period of time sufficient to allow protection against the lethality of the drug to develop. Large challenging doses of the same drug affected the thus protected rats, but the effects were reversible. Neutral lipids accumulated in the livers of both protected and control rats up to 18 hr at the same rates. After 18 hr, the levels in protected rats diminished, whereas in unprotected rats, liver fat accumulated continually until death. Administration of small protective doses raised SGOT for 48 hr, after which it normalized. A challenge dose caused another transient rise in SGOT in protected animals. In unprotected rats, the rise in SGOT continued progressively until death. In untreated rats, a nonlethal dose produced maximum or near-maximum increases in liver weight for 12-24 hr, and a maximum increase in liver neutral lipid accumulation up to 12 hr. No carbon tetrachloride was detected in whole rat blood 12 hr after protective doses were administered. After lethal doses, whole blood concentration reached maximum at 4 hr, and then declined. The liver content of carbon tetrachloride was much greater than the content in whole blood at 12 hr after administration of a large dose. However, 12 hr after administration of a small or a large dose, the same amount of carbon tetrachloride was bound to total liver lipids.

6469 QUANTITATIVE CHANGES IN GLYCOGEN IN THE RAT LIVER AFTER TETRACYCLINE.

(Ger.) Proksova, E. G. (Med. Fac., Comenius Univ., Martin, Czechoslovakia). *Anat. Anz.* 134(1/2):87-93, 1973.

In female Wistar rats, administration of a single dose of 50 mg/kg tetracycline i.m. increased glycogen deposition in the liver, primarily in the centroacinar region. This increase reached a maximum 10 hr after tetracycline injection. After 24 hr the quantity of glycogen deposited in the liver was about the same as that observed after 10 hr, but deposits were primarily located in cells under the capsule. A gradual decrease occurred in the number of glycogen-containing cells and in the quantity of glycogen they contained after injection of a single dose of 100 mg/kg tetracycline i.m. Administration of tetracycline (50 mg/kg i.m.) for 7 days produced a pronounced increase in glycogen deposition in the liver, but an even greater increase was obtained in rats who also received 2.5 ml of a 40% glucose solution. This suggests that tetracycline acts by blocking enzymes that inhibit glycogen hydrolysis rather than by stimulating glycogen synthesis.

6470 A METHOD FOR MEASURING DNA DAMAGE AND REPAIR IN THE LIVER IN VIVO. *(E.)* Cox, R.; Damjanov, I.; Abanobi, S. E.; Sarma, D. S. R. (Temple Univ. Sch. Med., Philadelphia, Pa.). *Cancer Res.* 33(9):2114-2121, 1973.

Alkaline sucrose gradients were used to study the induction of single-strand breaks in and repair of liver DNA *in vivo* in white male Wistar rats. Liver DNA was labeled during regeneration after partial hepatectomy. DNA was isolated from the organ in such a way as to minimize the induction of breaks due to handling or enzymatic activity. Different methods of preparing high-molecular-weight liver DNA were compared. Best results were obtained by squashing the liver in an ethylenediaminetetraacetic acid-sodium chloride buffer. Using this technique and alkaline sucrose gradients, high-molecular-weight DNA was regularly obtained. This DNA behaved like single-stranded DNA on hydroxyapatite columns and contained no detectable contamination of protein or RNA. It was thus demonstrated that hepatic DNA damage was produced within 4 hr by the administration of methyl methanesulfonate (120 mg/kg, i.p.) and that the rat can repair such hepatic DNA damage *in vivo* within 48 hr.

6471 COMPARISON BETWEEN *o*-AMINOPHENOL GLUCURONIDATION IN LIVER SLICES AND HOMOGENATES FROM CONTROL AND PHENOBARBITAL-TREATED WISTAR AND GUNN RATS. *(E.)* Winsnes, A.; Dutton, G. J. (Med. Sci. Inst., Univ. Dundee, Scotland). *Biochem. Pharmacol.* 22(14):1765-1771, 1973.

Glucuronidation rates were studied in sliced and homogenized liver from control and phenobarbital-treated Gunn and Wistar rats of both sexes; aglycone concentration was not significantly rate-limiting. Kinetic parameters of *o*-aminophenol uridine 5'-diphosphate glucuronyltransferase were determined in fresh (native) homogenates and those activated by uridine 5'-diphosphate-N-acetylglucosamine, digitonin, and diethylnitrosamine added singly or together. Apparent K_{UDP}-glucuronate-values were increased by both uridine 5'-diphosphate-N-acetylglucosamine and digitonin, but not by the specific activator diethylnitrosamine; values were similar for both strains and not significantly affected by phenobarbital pretreatment; sex differences were encountered. Apparent V_{max}-values were increased by 30- to 65-fold for Wistar and 400- to 1600-fold for Gunn rats in maximally-activated homogenates. Phenobarbital pretreatment approximately doubled V_{max} of maximally activated enzyme in all animals, but had little effect on V_{max} of native or partially-activated preparations. Slices of Gunn rat liver glucuronidated *o*-aminophenol at rates 30-44% those of Wistar rats; rates in both strains exhibited a consistent sex difference and increased after phenobarbital treatment. Comparison of results from slices and homogenates containing physiological concentrations of uridine 5'-diphosphate-glucuronate suggested that in both sexes and strains uridine 5'-diphosphate-glucuronyltransferase activity *in vivo* is higher than that observed in native unactivated homogenates, presumably because of endogenous activators; however, as glucuronidation in similar, but maximally-activated, homogenates was well above that in slices, the enzyme may still remain partially latent *in vivo*.

6472 BILE ACID FORMATION BY LIVER MICROSOMAL SYSTEMS. *(E.)* Greim, H.; Trulzsch, D.; Czygan, P.; Hutterer, F.; Schaffner, F.; Popper, H.; Copper, D. Y., Rosenthal, O. (Mount Sinai Sch. Med., City Univ. New York, N.Y.). *Ann. N.Y. Acad. Sci.* 212:139-147, 1973.

Several steps in bile salt metabolism involve ring hydroxylation by microsomal cytochrome P-450. That this cytochrome participates in 7α-hydroxylation of deoxycholate and 6β-hydroxylation of chenodeoxycholate is shown by the maximal reversibility of the carbon monoxide-inhibited reactions by monochromatic light at 450 nm. In rats, 7α-hydroxylation of deoxycholate reconverts this secondary bile salt to cholate, but in man this pathway is little used. The P-450-dependent 6β-hydroxylation of chenodeoxycholate to form muricholic acids is enhanced in cholestatic rat liver. This hydroxylation step is protective, since β-muricholate is less hepatotoxic than chenodeoxycholate. No β-muricholate is found in man. Instead, cholate concentration increases in human cholestasis, which involves 12α-hydroxylation. The P-450 dependency of this last reaction is not established. Enhanced cholate formation may protect the human liver from dihydroxy bile salts, which exert detergent action and accumulate in prolonged cholestasis, but this protection is less effective than that provided by the P-450-dependent mechanism in the rat.

6473 CHANGES IN CHOLERESIS IN THE UNRESTRAINED WAKING RAT AFTER REESTABLISHMENT OF THE

ENTEROHEPATIC CYCLE. *(Fr.)* Labrid, C.; Dureng, G. (Dept. Gastroenterol. Pharmacol., C.E.R.M., Riom, France). *J. Pharmacol. (Paris)* 4(2):279-282, 1973.

Total bile flow and bilirubin and bile salt outputs were measured in unrestrained waking rats with bile fistulas. Loss of bile constituents through the bile fistula was corrected by connecting the rat to a donor animal with a bile fistula. Administration of 1-phenyl-1-hydroxy-n-pentane increased total bile flow by a maximum of 84%, increased bilirubin output by a maximum of 33%, but had no effect on bile salt output. Dehydrocholic acid had no effect on total bile flow, but increased bilirubin output by a maximum of 75% and bile salt output by a maximum of 77%. Phenyldimethylacetic acid increased total bile flow by a maximum of 143%, bilirubin output by a maximum of 142%, and bile salt output by a maximum of 50%.

6474 INTERACTION OF SERUM ALBUMIN AND BILIRUBIN AT LOW CONCENTRATIONS. *(E.)* Clarenburg, R.; Barnhart, J. L. (Dept. Physiol. Sci., Kansas State Univ., Manhattan). *Am. J. Physiol.* 225(2):493-496, 1973.

Buffered mixtures of bilirubin-^{14}C and bovine serum albumin (molar ratios 0.04-1.5) were ultracentrifuged; nonalbumin-bound bilirubin-^{14}C was assayed in the supernatants. At a given albumin level, unbound bilirubin constituted a constant proportion of variable bilirubin concentrations. The proportion remained constant with molar ratios of bilirubin to albumin from 0.04 to 1.5. Doubling the albumin concentration from 0.75 to 1.5% and again to 3.0% reduced the fraction of bilirubin remaining unbound by a 1.36 factor. To conform that finding with the law of mass action, a constant level of active bilirubin binding sites ([AS$^+$]) in the albumin solution had to be proposed: for each AS$^+$ occupied, a new AS$^+$ is generated. Though [AS$^+$] thus would be proportional to albumin concentration, doubling the albumin level did not double [AS$^+$] , but increased [AS$^+$] by only about 1.414. This indicates that in the process of generating AS$^+$ another factor, designated I, was simultaneously produced. A model was proposed for albumin-bilirubin intreaction: bilirubin-binding to AS$^+$ (equilibrium K_1) changes the tertiary structure of albumin exposing potential binding sites (ASI) in equilibrium (K_2) with active sites AS$^+$ and factor I. The proposed model, based on ultracentrifugally defined equilibria, is consistent with reported physicochemical observations on albumin-bilirubin complexes, and is supported by observed kinetics of bilirubin uptake in isolated perfused livers.

6475 USE OF THIN-LAYER CHROMATOGRAPHY AND SPECTROPHOTOFLUORIMETRY FOR QUANTITATIVE DETERMINATION OF CONJUGATED BILE ACIDS LIBERATED AFTER HYDROLYSIS. *(Ger.)* Bruhl, W.; Schmid, E. (Med. Acad., Lubeck, Germany). *Z. Gastroenterol.* 10(1): 40-43, 1972.

A technique has been developed for quantitative determinations of bile acids in bile, serum, and liver homogenates. After precipitation of protein in acetone:ethanol (1:1) or chloroform:methanol (2:1), centrifugation, concentration of the residue, and hydrolysis of the dry residue with NaOH, samples were treated by the Frosch method and aliquots of extract were applied to thin-layer plates of kieselguhr and eluted with isoocytane:ethylacetate:acetic acid (60:30:12). After spraying with 5% H_2SO_4 in methanol and heating for 20 min at 95 C, fluorescence was measured directly on the plate with a spectrophotofluorimeter. This method is sensitive for as little as 0.2 μg bile acid and the results are reproducible. Hydrolysis caused a 10-20% loss of conjugated bile acids. Tables are presented to show the quantities of cholic, deoxycholic, and chenodeoxycholic acids in serum from patients with no evidence of liver disease and from those with cirrhosis, acute hepatitis, and chronic hepatitis and in liver homogenate and gallbladder bile from cadavers.

6476 BILE SECRETION AND ^{131}I-BSP EXCRETION IN ANIMAL BILE AFTER SPIRONOLACTONE TREATMENT. *(Ger.)* Gerstner, L.; Hayr, A.; Mostbeck, A.; Peschl, L.; Svrcek, G.; Neumayr, A. (Empress Elisabeth Hosp., Vienna, Austria). *Z. Gastroenterol.* 10(7): 555-560, 1972.

Bile flow, ^{131}I-BSP excretion in gallbladder bile, and changes in liver weight were measured on 10 male Wistar rats given spironolactone (4 mg twice a day for 4 days i.p.) and on 10 controls given i.p. injections of physiological saline. Spironolactone significantly increased bile flow, ^{131}I-BSP in gallbladder bile. Liver weights of spironolactone-treated rats were somewhat higher than those of controls, but the difference was not statistically significant. These findings show that the increased excretion of ^{131}I-BSP in the bile of spironolactone-treated rats is not due to the increase in bile flow, but to an increase in the glucuronic acid conjugation of BSP by enzyme activation.

6477 CHOLESTEROL: VITAMIN C CONTROLS ITS TRANSFORMATION TO BILE ACIDS. *(E.)* Ginter, E. (Inst. Human Nutr. Res., Bratislava, Czechoslovakia). *Science* 179(4074):702-704, 1973.

The rate of cholesterol conversion to bile acids was studied in 52 guinea pigs with latent vitamin C deficiency. Normal body growth was not affected by latent hypovitaminosis C. However, the concentration of vitamin C in the liver and spleen of the deficient animals was 1.6 and 4.7 mg/100 g, resp., compared with 8.2 and 21.6 mg/100 g, resp., in controls. Cholesterol content rose from 126-218 mg/100 ml in the serum and from 359-443 mg/100 g in the liver. Latent hypovitaminosis C reduced the rate of cholesterol to bile acids transformation from 11.8-8.3 mg/24 hr/500 g. It is stressed that these results were obtained from animals with latent vitamin C deficiency, not acute scurvy. These results show that the higher the vitamin C concentration in the liver, the lower the cholesterol concentration in liver and serum, indicating that the cholesterol content is controlled by the rate of cholesterol conversion to bile acids. This conversion takes place in the liver, and the rate of conversion apparently depends on the vitamin C concentration in the liver cells. It is suggested that latent hypovitaminosis C may cause hypercholesteremia in humans and may also be important in the pathogenesis of atherosclerosis.

6478 7α-HYDROXYLATION OF TAURODEOXYCHOLIC ACID BY A RECONSTITUTED SYSTEM FROM RAT LIVER MICROSOMES. *(E.)* Bjorkhem, I.; Danielsson, H.; Wikvall, K. (Dept. Chem., Karolinska Inst., Stockholm, Sweden). *Biochem. Biophys. Res. Commun.* 53(2):609-616, 1973.

A reconstituted system consisting of partially purified cytochrome P-450 and cytochrome P-450 reductase from liver microsomes of male Sprague-Dawley rats catalyzed an efficient 7α-hydroxylation of taurodeoxycholic acid in the presence of a reduced nicotinamide adenine dinucleotide phosphate-generating system. Addition of phosphatidyl choline slightly stimulated the reaction. The system had a low capacity to 6β-hydroxylate taurochenodeoxycholic acid and lithocholic acid.

6479 EXTRACORPOREAL ASSIST OF ANHEPATIC ANIMALS WITH LIVER SLICE PERFUSION. *(E.)* Soyer, T., Lempinen, M.; Walker, J. E., Supanwanid, P.; Eisman, B. (Denver Gen. Hosp., Colo.). *Am. J. Surg.* 126(1):20-24, 1973.

Thin (0.5 to 1.0 mm) liver slices perfused with arterial blood were used to provide temporary support of 9 anhepatic pigs. Liver slice assist was instituted 2 hr after hepatectomy in 4 animals and 18-24 hr after operation in the remaining 5. The extracorporeal perfusion technique is far simpler than whole liver perfusion. Evidence of its effectiveness included a return toward normal electroencephalogram tracings, urea production, and bilirubin conjugation. However, the limited length of survival on liver slice assist (mean of 30 hr) and the ultimate relapse into coma indicate that the technique is not yet capable of providing total support.

6480 GLUTAMYL TRANSFERASE IN THE SERUM AND LIVER DURING EXPERIMENTAL LIVER DAMAGE. *(Ukr.)* Hromashevs'ka, L. L.; Sylakova, A. I.; Ilashchuk, Y. D.; Kasatkina, M. G. (Inst. Infect. Dis., Kiev, USSR). *Ukr. Biokhim. Zh.* (3):290-294, 1972.

Glutamyl transferase (GAT) activity was measured in the serum and liver of male albino rats and white mice before and 2-48 hr after administration of a single dose of carbon tetrachloride (CCl_4). Acute liver damage was induced in mice and rats by injection of 0.5 ml/100 g s.c. and 0.5 or 0.2 ml/100 g s.c., resp. In mice a single injection of CCl_4 significantly increased serum GAT and significantly decreased liver GAT activity. The maximum decrease in liver GAT activity occurred after 24-48 hr, and the maximum increase in serum GAT activity after 20 hr. Changes in the activity of GAT paralleled changes in the activity of aspartate aminotransferase and, more closely, those of alanine aminotransferase. Similar dose-dependent changes occurred in GAT activities in rats. Liver GAT activity decreased to about 1/3 of its normal value after 0.2 ml/100 g CCl_4 and to less than 1/3 of its normal value after 0.5 ml/100 g; serum GAT activity increased to 150-250 times its normal value. In rats and mice with postnecrotic cirrhosis, induced by prolonged injection of CCl_4 (0.5 ml/100 g s.c. every 3 days for 2.5-3 months) and in rats with biliary cirrhosis induced by ligation of the common bile duct for 1-2 months, the GAT activity decreased by an average of 63% in the liver but remained relatively unchanged in serum. Serum GAT activities were significantly increased in 90 patients with infectious hepatitis, remained unchanged in 3 patients with cirrhosis, and were significantly increased in 9 patients with chronic hepatitis. These findings suggest that the same mechanism may be involved in changes occurring in serum GAT, SGOT, and SGPT activities in liver damage. Decreases in the GAT activity and glutamine content of the liver in liver damage may result from decreases in the activity of enzymes which take part in the biosynthesis of glutamine. This is very likely true for glutamine synthetase which forms a functional complex with glutamine transferase; the activity of the latter enzyme decreases markedly in liver damage.

6481 CHANGES IN RATE OF ETHANOL ELIMINATION ASSOCIATED WITH CHRONIC ADMINISTRATION OF ETHANOL TO CHIMPANZEES AND RHESUS MONKEYS. *(E.)* Pieper, W. A.; Skeen, M. J. (Yerkes Regional Primate Res. Ctr., Atlanta, Ga.). *Drug Metab. Disposition* 1(4):634-641, 1973.

Ethanol elimination increased in 7 young chimpanzees and 3 rhesus monkeys during 6-29 weeks of chronic ethanol administration. Ethanol dose levels were increased from 2-3 to 6-9 g/kg/day. Blood ethanol levels were measured after ethanol was given mixed with a liquid high-protein, low fat formula, *via* a nasogastric tube, or by i.v. infusions of ethanol dissolved in physiological saline. In both species the increase in the rate of elimination was dose related and independent of the duration of ethanol administration. Elevated elimination rates returned to baseline values during abstinence, indicating that the changes in the elimination rate were directly related to ethanol administration. Measurements in 4 chimpanzees receiving no ethanol indicated that no systematic changes in the elimination rate occurred as the young animals developed. In both species blood ethanol levels peaked 1.5-2.5 hr after p.o. or nasogastric administration except when doses were larger than 3 g/kg. No difference was observed in elimination rates in chimps when ethanol was administered p.o. and i.v. In 6 chimps the mean percentage of increase in elimination rates attained by the end of each chronic administration period was 44.2%, for rhesus monkeys it was 101.6%. These results indicate that if sufficient ethanol is administered on a chronic schedule, the rate of ethanol elimination is increased. If moderate amounts of ethanol are consumed even for extended periods, no such increase occurs. As elimination rates increase, larger amounts of ethanol are required to maintain the presence of the drug in the body fluids and to sustain physiological and behavioral effects.

6482 MECHANISM OF LITHOGENIC BILE PRODUCTION: STUDIES IN THE HAMSTER FED AN ESSENTIAL FATTY ACID-DEFICIENT DIET. *(E.)* Robins, S. J.; Fasulo, J. (Boston VA Hosp., Mass.). *Gastroenterology* 65(1):104-114, 1973.

The essential fatty acid-deficient hamster forms lithogenic hepatic bile and gallstones with a high cholesterol content. Measurements of bile acid kinetics and biliary lipid secretion have been performed in this animal model to determine if bile becomes lithogenic as a result of an absolute increase in cholesterol or as a consequence of a primary decrease in cholesterol-solubilizing lipids. An essential fatty acid-deficient diet prolonged the turnover, increased reabsorption, and decreased synthesis of cholic acid. The pool size of cholate was, however, the same as in chow-fed controls, both before and after gallstone development. Biliary secretion rates were determined in nonfasted animals from the first 30-min bile collection after common duct cannulation. An essential fatty acid-deficient diet did not decrease total bile salt or phospholipid output. In contrast, biliary cholesterol secretion in these hamsters was 2 to 3 times higher than in controls, and was significantly elevated prior to stone development. In essential fatty acid-deficient hamsters, cystic duct ligation to exclude the gallbladder from the enterohepatic circulation produced an even greater elevation of cholesterol secretion, but did not influence the secretion rate of bile salt or phospholipid. In these hamsters increased biliary cholesterol secretion was not associated with an increase in serum, liver, or whole carcass cholesterol levels. Thus, the production of lithogenic bile in the essential fatty acid-deficient hamster is clearly a consequence of selective enhancement of biliary cholesterol secretion, not eliminated by gallbladder exclusion, and not associated with a generalized increase in body cholesterol levels.

6483 CYTOCHROME c STIMULATED OXIDATION OF ETHANOL BY LIVER MITOCHONDRIA. *(E.)* Kiessling, K. H.; Pilstrom, L. (Inst. Zoophysiol., Univ. Uppsala, Sweden). *Biochem. Pharmacol.* 22(18): 2229-2235, 1973.

The addition of ethanol (1.7-17.0 μM/liter), nadide, alcohol dehydrogenase, and cytochrome c to liver mitochondria of male Wistar rats gives rise to an oxygen consumption proportional to the amount of ethanol oxdized. The system is insensitive to rotenone and antimycin and not coupled to phosphorylation and is in these respects identical with the well-known reduced nicotinamide adenine dinucleotide (NADH)-cytochrome c reductase present in the outer membrane of liver mitochondria. The respiration is directly proportional to the added cytochrome c (1.6-16.3 μM/liter) and follows the Michaelis-Menten equation for different ethanol concentrations (K_m = 6.2 μM/liter). As cytochrome c is easily washed out of mitochondria during fractionation, the externally added cytochrome c probably replaces it *in vitro*. Therefore, cytochrome c may alternate between the outer and inner membrane and may be available *in vivo* for the oxidation of extramitochondrial NADH by means of the NADH-cytochrome c reductase in the outer membrane.

6484 CHOLESTEROL SOLUBILITY IN BILE. EVIDENCE THAT SUPERSATURATED BILE IS FREQUENT IN HEALTHY MAN. *(E.)* Holzbach, R. T.; Marsh, M.; Olszewski, M.; Holan, P. (St. Luke's Hosp., Cleveland, Ohio). *J. Clin. Invest.* 52:1467-1479, 1973.

Direct measurement of maximum biliary cholesterol solubility in 5 large mammalian species, including man, revealed a micellar zone significantly smaller than that previously reported. Further studies on *in vitro* model solutions patterned after bile confirmed in this new micellar zone. Thus, the micellar zone boundary derived *in vitro* from model solutions is applicable to human gallbladder bile. Using the present criteria, human bile from patients without biliary tract disease, in contrast to bile from other mammalian species, is supersaturated with cholesterol. A male-female difference in bile composition is not demonstrable despite the well-established female preponderance of cholelithiasis. Bile from most patients with cholesterol cholelithiasis has a micellar zone similar to normals but has greater excess of cholesterol above saturation. It is concluded that cholesterol supersaturation may be a necessary but not solely sufficient cause for gallstone formation.

6485 THE EFFECTS OF STARVATION ON THE PROLIFERATIVE RESPONSE AFTER PARTIAL HEPATECTOMY. *(E.)* Stirling, G. A.; Laughlin, J.; Washington, S. L. A. (Univ. Nottingham Med. Sch., England). *Exp. Mol. Pathol.* 19(1):44-52, 1973.

The incidence of mitoses/1000 lymphocytes was used as a measure of liver regeneration after partial hepatectomy in male Wistar rats starved before and after operation. Two groups of rats were starved for 48 and 72 hr, resp., before 67% partial hepatectomy involving resection of the anterior lobes; a small group was starved for 72 hr before 30% partial hepatectomy in which only the left lateral lobe was removed. In animals starved 48 hr before operation, the initial evidence of postoperative proliferative activity was delayed 5 hr after which the response steadily increased but without reaching the value obtained for fed animals. Inhibition of the proliferative response was more marked and the mitotic index further depressed when the period of starvation before partial hepatectomy was 72 hr. The inhibition was not affected by administration of glucose or glucagon nor by reducing the severity of the operation. Delayed DNA synthesis in some starved rats was demonstrated by the delayed incorporation of tritium-labeled thymidine (0.5 μCi/g) given 20 hr after operation. Thus, factors responsible for inhibition of the proliferative response operate early in the mitotic cycle and delay DNA synthesis.

6486 EFFECT OF FATTY ACIDS ON BILIRUBIN CONJUGATION.

(E.) Hargreaves, T. (Area Pathol. Lab., Exeter, England). *Arch. Dis. Child.* 48(6):446-450, 1973.

The effects of fatty acids on bilirubin conjugation were studied using liver slices from male albino Wistar rats. Saturated fatty acids containing 4-20 carbon atoms did not inhibit conjugation when added at concentrations of 1 or 10 mM/liter. Unsaturated C_{18} and C_{20} fatty acids (1 to 10 mM/liter) inhibited bilirubin conjugation in liver slices and in microsomes. The inhibition generally increased with the degree of unsaturation. γ-linoleic acid was the most effective of the C_{18} unsaturated acids and 5,8,11,14,17-eicosapentaenoic the most effective of the C_{20} unsaturated acids. It is suggested that an unusually high concentration of one of the unsaturated acids in maternal milk may be a factor in producing breast milk jaundice.

6487 PHENOBARBITAL-INDUCED FATTY LIVERS IN THE RAT.

(E.) Sorrell, M. F.; Tuma, D. J.; Noffsinger, J. K.; Barak, A. J.; Baker, H. (Univ. Nebraska Sch. Med., Omaha). *Proc. Soc. Exp. Biol., Med.* 143(3):839-843, 1973.

Administration of phenobarbital (50 mg/kg, i.p., every 12 hr for 5 days) to Sprague-Dawley rats fed a standard laboratory diet or 6 different synthetic diets produced elevated levels of triglyceride, phospholipid, and total cholesterol in the livers of these animals. Triglycerides appeared to be more influenced by dietary levels of choline and fat than phospholipids and cholesterol. Regardless of dietary fat or choline levels, phenobarbital produced approximately the same increase in phospholipid and total cholesterol levels. Increasing protein levels in the diet did not change the effect of phenobarbital on liver fats. The data suggest that the mechanism of action of phenobarbital in inducing hepatic triglyceride accumulation may be partially mediated through the metabolic process which renders choline lipotropic.

6488 BIOCHEMICAL AND HISTOMORPHOLOGICAL CHANGES IN EXPERIMENTAL PORPHYRIA INDUCED BY HEXACHLOROBENZENE.

(Ger.) Iwanow, E.; Hlebarowa, M.; Krustev, L.; Dimitrov, P.; Orbetzova, V.; Nenov, P.; Kirjakov, A.; Tsontscheva, A. (Inst. Nutrition Res., Sofia, Bulgaria). *Acta Hepatogastroenterol.* 20(1): 39-48, 1973.

Histological, enzymological, and biochemical changes were studied in the livers of male Wistar rats during and after addition of hexachlorobenzene (0.4 g/100 g/day) to their food. In contrast to severe clinical symptoms of intoxication, only mild dystrophic changes developed in the liver; no evidence of cholestasis or necrosis was ever found. LDH and malate dehydrogenase (MDH) activities decreased in the liver while the activity of alkaline phosphatase increased significantly by the 11th day and decreased on the 15th day after addition of hexachlorobenzene. No changes occurred in SGOT, SGPT, or serum alkaline phosphatase activities. The metabolism of porphyrin and its precursors was greatly disturbed. Under UV light the characteristic purple-red fluorescence of porphyrins appeared on the muzzle, teeth, tissues around the eyes, and nasal secretion in all animals, but none of the viscera were fluorescent at autopsy. After 7 days ∂-aminolevulinic acid, uroporphyrin, and coproporhyrin levels increased in the urine and feces, reached a high on the 11th day, and decreased again on the 15th day. The levels of all porphyrins reached a maximum 30 days after discontinuation of hexachlorobenzene. Significant decreases occurred in the contents of nicotinamide adenine dinucleotide (NAD) and reduced nicotinamide adenine dinucleotide (NADH) in the liver, but the ratio NAD/NADH increased, reaching a maximum 30 days after discontinuation of hexachlorobenzene. The pyruvate content of the liver had decreased to about 1/2 of its initial level after 11 and 15 days, but no change occurred in the liver lactate content or the lactate/pyruvate ratio. The lactate-pyruvate system and LDH activities normalized 30 days after discontinuation of hexachlorobenzene, while MDH activity was still significantly decreased. On the 11th day the ATP content of the liver was decreased, while that of ADP was increased; these changes were less apparent on the 15th day, but the AMP content was reduced.

6489 STUDIES ON THE FORMATION OF C_7-OXYGENATED CHOLESTEROL AND β-SITOSTEROL METABOLITES

IN CELL-FREE PREPARATIONS OF RAT LIVER. *(E.)* Aringer, L.; Eneroth, P. (Dept. Chem., Karolinska Inst., Stockholm, Sweden). *J. Lipid Res.* 14(5):563-572, 1973.

The microsomal fraction and the 18,000 *g* supernatant fluid obtained from livers from normal male Sprague-Dawley rats, cholestyramine-treated rats, or from rats with a bile fistula were used to compare the 7 α-hydroxylation of [4-^{14}C]cholesterol and β-[4-^{14}C]sitosterol (24 α-ethyl-cholesterol). The specific formation of 7 α-hydroxy-β-sitosterol was not increased above 0.05% with any of the preparations. This was less than 1% of the conversion found for cholesterol. The inhibitory effect of added 7-oxo and 7 β hydroxy-β-sitosterol on the 7 α-hydroxylation of cholesterol was much less than that of the corresponding cholesterol compounds. 7 α-Hydroxy-β-sitosterol was without effect. It is concluded that the activity of the cholesterol 7 α-hydroxylase depends on the structure of the steroid side chain. No discrimination of 7 β-hydroxy-β-sisterol compared with 7 β-hydroxycholesterol occurred upon oxidation to the 7-oxo compounds; but a persistent difference in the degree of reduction of the 7-oxo derivatives was noticed, indicating the presence of 2 separate steroid C_7 oxidoreductases in the rat liver 18,000 *g* supernatant fluid.

6490 SIGNIFICANCE AND CAUSES OF HISTAMINE RELEASE DURING ORTHOTOPIC HOMOLOGOUS LIVER TRANSPLANTATION IN THE PIG. *(E.)* Lorenz, W.; Boeckl, O.; Struck, E.; Hell, E.; Zimmermann, G.; Reimaan, H. J.; Tauber, R.; Scheffer, B. (Surg. Clin., Univ. Marburg/Lahn, Germany). *Agents Actions* 3(1):2-11, 1973.

The acute arterial hypotension occurring in the revascularization phase of orthotopic homologous liver transplantation in pigs was greatly diminished by the administration of chlorphenoxamine (2 mg/kg). A 3-4 fold increase of the plasma histamine concentration during this phase of operation and a strong hypotensive effect of corresponding plasma histamine levels in pigs, as determined after injection of 48/80, suggest that histamine release may contribute to critical circulatory situations during liver transplantations. Anesthesia, manipulations at the stomach and gut, passage of the blood through the extracorporeal bypass and the ischemia followed by a sudden warming of the liver were shown as possible causes of histamine release in various degrees during this operation. The role of other vasoactive substances and of biophysical mechanisms for the development of hypotension in the revascularization phase cannot yet be determined.

6491 ALTERATIONS IN BILIARY LIPIDS OF MICE DURING DEHYDROCHOLIC ACID FEEDING. DiTullio, N. W.; Stack, E. J. (Smith, Kline & French Labs., Philadelphia, Pa.). *J. Lipid Res.* 14(5):552-556, 1973.

Female Charles River mice were fed a lithogenic diet consisting of Purina chow and 0.5% dehydrocholic acid. Controls received Purina chow. Every 2 weeks for 20 weeks animals were killed, and biliary phospholipid, cholesterol, and bile salt concentrations were determined, as well as the extent of gallstone formation. With time there was a gradual, significant decline in the concentration and the relative composition of phospholipid in both groups compared with initial values. There was a significant increase in biliary cholesterol concentration and relative amount in the group on the lithogenic diet. The average difference in cholesterol concentration between the groups was 6.5 μMs/ml. No significant differences were found in the relative amounts of bile salt or phospholipid between the two groups. Feeding dehydrocholic acid resulted in increased concentrations of bile salts. This increase was significant only at the 12th week; however, the average increase over the 2nd to 20th week was 18 μMs/ml. The sum of measured lipid was increased 27 μMs/ml. After 8 weeks, gallstones were found in approximately 60% of autopsied animals and correlated with increased cholesterol concentration. These data support the hypothesis that there is a component of cholesterol secretion which may not be bile salt- or phopholipid-dependent. These data also suggest that biliary phospholipid secretion decreases with age.

6492 THE ROLE OF DIETARY PROTEIN IN GENERATING DAILY RHYTHMS IN RAT LIVER TRYPTOPHAN PYRROLASE AND TYROSINE TRANSAMINASE. *(E.)* Ross, D. S.; Fernstrom, J. D.; Wurtman, R. J. (Dept. Nutr., Massachusetts Inst. Technol., Cambridge). *Metabolism* 22(9):1175-1184, 1973.

Groups of male Sprague-Dawley rats were exposed to light for 12 hr daily, given access to either an 18% casein diet or a protein-free diet at different times of day or night, and sacrificed after 24 hr. Tryptophan pyrrolase activity rose significantly (34-67%) during the dark period in all animals. However, tyrosine transaminase activity rose during the dark period (163%) only among those eating protein. In rats eating a protein-containing chow diet in the afternoon following an overnight fast, analysis 2 or 4 hr later showed that tryptophan pyrrolase activity did not increase after food consumption, but tyrosine transaminase activity rose 120-140%. If animals ate chow for 12 hr/day, starting either at the onset of darkness or 6 hr later, the daily increases in tryptophan pyrrolase began several hours before animals were given access to food rather than after food ingestion, while the daily increases in tyrosine transaminase were always noted immediately after eating. Therefore, the cyclic ingestion of dietary protein is extremely important in generating the tyrosine transaminase rhythm, but is of little significance in producing the tryptophan pyrrolase rhythm. Variations in plasma tryptophan concentration did not correlate well with tryptophan pyrrolase activity in any group fed a diet containing protein. Plasma tryptophan concentrations did not rise prior to the increases in tryptophan pyrrolase activity, nor did they fall after these increases. Thus, the normal daily rhythm in tryptophan pyrrolase activity apparently neither results from nor elicits the plasma tryptophan rhythm.

6493 PREVENTION OF THE HEPATOTOXIC EFFECTS OF D-GALACTOSAMINE BY D-GALACTOSE. *(E.)*

Mexzaros, K.; Antoni, F.; Hrabak, A.; Szikla, C.; Garzo, T.; Tompa, A.; Lapis, K. (Inst. Med. Chem., Budapest, Hungary). *F.E.B.S. Lett.* 35(1):1-3, 1973.

Liver morphology was examined in white male CFLP mice starved for 12 hr. Physiological saline was injected into controls, 7 mice received D-galactosamine (1 g/kg) and another 7 received D-galactosamine (1 g/kg) and D-galactose (2 g/kg), i.p. The mice were sacrificed after 18 hr. Necrotic changes in the livers of the D-galactosamine treated rats were revealed by light microscopic examination of liver sections stained with hematoxylin-eosin. No necrosis was found in the livers of animals receiving both D-galactosamine and D-galactose. This study suggests that D-galactose abolishes various toxic effects of D-galactosamine *in vitro* and *in vivo*. The significance of non-*N*-acetylated uridine diphosphate-hexosamines in D-galactosamine toxicity is strongly supported by these findings.

6494 EFFECT OF ETHANOL ON RATES OF ELIMINATION AND METABOLISM OF ZOXAZOLAMINE, HEXOBARBITAL AND WARFARIN SODIUM IN THE RAT. *(E.)*

Mallov, S.; Baesl, T. (State Univ. New York, Upstate Med. Ctr., Syracuse). *Biochem. Pharmacol.* 21(12):1667-1678, 1972.

Male Sprague-Dawley rats were fed single doses of ethanol (4.71 g/kg, i.v.) or isocaloric quantities of glucose, in solution, by stomach tube following a 6 hr fast and were injected with zoxazolamine (25 mg/kg), warfarin sodium (1.5 or 3 mg/kg, i.v.), or hexobarbital (100 mg/kg, i.p.) 2 or 17 hr later. Other rats were pair-fed a nutritionally adequate synthetic diet containing ethanol or isocaloric quantities of sucrose for 7-11 days, and were treated with drugs following a 17 hr fast. Plasma concentrations of each drug were determined at various intervals of time following the injections. Administration of one dose of ethanol significantly increased the rates of elimination of zoxazolamine and of hexobarbital from the circulation 17 hr later, but the rate of warfarin elimination was unchanged. Chronic ethanol feeding also increased the rate of zoxazolamine elimination; but this increase was not greater than that following acute ethanol feeding; warfarin elimination was again not altered. Rates of metabolism of the drugs by liver microsomes *in vitro* 17 hr after a single dose of ethanol or glucose mirrored the effects on elimination *in vivo;* they were significantly increased in the alcohol-treated rats in the case of zoxazolamine and hexobarbital, but not changed in the case of warfarin. The rates of elimination of zoxazolamine and warfarin from the circulation were significantly reduced in rats fed ethanol 2 hr before. It is concluded that acute ethanol intake may increase the rates of elimination of some drugs when the alcohol is no longer present, as a consequence of microsomal enzyme induction, and may decrease rates of drug elimination when alcohol is present *in vivo*, probably as a result of inhibition by ethanol of microsomal drug-metabolizing enzymes.

6495 REGULATION BY DIETARY CHOLINE OF HEPATIC FATTY ACID SYNTHETASE IN THE RAT. *(E.)*

Rosenfeld, B. (Banting and Best Dept. Med. Res., Univ. Toronto, Canada). *J. Lipid Res.* 14(5):557-562, 1973.

Fatty acid synthetase activity was measured in the high-speed supernatant fraction of liver homogenates from male albino rats fed a semisynthetic diet low in lipotropic factors. When choline was omitted from the diet, fatty acid synthetase activity, expressed as nmoles reduced nicotinamide adenine dinucleotide phosphate oxidized/min, increased from 7.8-32.6 after 2 feedings of the deficient diet. This increase of fatty acid synthetase activity could account for the increased triglyceride accumulation in the hepatic floating lipid fraction of the same rats (341 mg/liver) *versus* controls (15.0 mg/liver). Gas-liquid chromatographic analysis of the floating lipid triglycerides showed an increased content of palmitic acid due to choline deficiency. This increase could be predicted from the increased fatty acid synthetase activity and its known characteristic yield of palmitic acid.

6496 COMPARATIVE CHANGES IN SERUM ENZYME LEVELS IN BERYLLIUM- OR CARBON TETRACHLORIDE-INDUCED LIVER NECROSIS. *(E.)*

Clary, J. J.; Groth, D. H. (Natl. Inst. Occupational Safety and Health, Cincinnati, Ohio). *Proc. Soc. Exp. Biol. Med.* 143(4):1207-1210, 1973.

Serum enzymes (isocitric dehydrogenase, SGOT, SGPT, LDH) and the liver enzyme, acid phosphatase, were used to evaluate the response in the rat to beryllium-induced midzonal liver necrosis and carbon tetrachloride-induced centrolobular necrosis. Beryllium produced a maximum elevation of liver free acid phosphatase 8 hr after injection. The elevation of the serum enzymes isocitric dehydrogenase, SGOT, or SGPT was not observed until 48 hr after beryllium injection. LDH was not elevated at any time. At equivalent doses in the carbon tetrachloride-injected animals, serum isocitric dehydrogenase, SGOT, and SGPT were all elevated by 48 hr, but no elevation of liver acid phosphatase was observed at any time. These responses indicate a biochemical as well as an anatomical difference between these 2 types of chemically-induced liver necrosis.

6497 REGULATORY EFFECTS OF STEROLS AND BILE ACIDS ON HEPATIC 3-HYDROXYL-3-METHYLGLUTARYL CoA REDUCTASE AND CHOLESTEROL 7α-HYDROXYLASE IN THE RAT. *(E.)* Shefer, S.; Hauser, S.; Lapar, V.; Mosbach, E. H. (Public Hlth. Res. Inst., New York, N.Y.). *J. Lipid Res.* 14(5):573-580, 1973.

Specific activities of the hepatic microsomal enzymes 3-hydroxy-3 methylglutaryl CoA (HMG CoA) reductase and cholesterol 7α-hydroxylase were studied in male Sprague-Dawley-derived rats fed sterols and bile acids. The administration of bile acids (taurocholate, taurodeoxycholate, taurochenodeoxycholate) at a level of 1% of the diet for 1 week reduced the activity of HMG CoA reductase. Taurocholate and taurodeoxycholate, but not taurochenodeoxycholate, inhibited cholesterol 7α-hydroxylase. Dietary sitosterol produced increases in the specific activity of HMG CoA reductase (3.6 fold) and cholesterol 7α-hydroxylase (1.4-fold), and more than doubled the biliary cholesterol concentrations in this group. Compared with controls fed the stock diet, the simultaneous administration of sitosterol and taurochenodeoxycholate resulted in a 60% decrease of HMG CoA reductase activity and no change in cholesterol 7α-hydroxylase activity or biliary cholesterol concentration. Rats fed sitosterol plus taurocholate had nearly normal HMG CoA reductase activity, but cholesterol 7α-hydroxylase was inhibited and biliary cholesterol remained high. Bile acid secretion rates and biliary bile acid composition were similar in controls and sterol-fed animals. In all groups receiving bile acids, biliary secretion of bile acids was nearly doubled and bile acid composition was shifted in the direction of the administered bile acid. It is concluded that the composition of the bile acid pool influences the hepatic concentrations of the rate-controlling enzymes of bile acid synthesis. These results support the hypothesis that bile acids inhibit HMG CoA reductase directly, not indirectly by stimulating cholesterol absorption and thereby increasing enterolymphatic cholesterol flux.

6498 TURNOVER OF BILE ACIDS IN THE HYPERCHOLESTEROLEMIC RAT AS INFLUENCED BY SATURATION OF DIETARY FAT. *(E.)* McGovern, R. F.; Quackenbush, F. W. (Tompkins Cty. Hosp. Lab., Ithaca, N.Y.). *Lipids* 8(8):466-469, 1973.

Injections of [24-^{14}C] chenodeoxycholate (0.5 μCi) and ^{3}H-cholate (1.7 μCi) were made by heart puncture into 300 g male Wistar rats that bore T-cannulas in their bile ducts. The animals had been raised on diet A, containing glucose, cholesterol, and cholate, or diet B, containing sucrose and cholesterol; each of the diets contained 5% safflower oil or 5% beef tallow as variables. Analysis of bile samples collected at intervals over a 5-day period showed that the safflower oil group fed diet B had a 17% shorter cholate half-life, a 29% larger cholate pool size and 52% higher rate of cholate synthesis than those fed beef tallow in the same diet. The safflower group fed diet A also had a larger cholate pool size, but synthesis and half-life were obscured by cholate feeding. Chenodeoxycholate turnover data were not obtainable because the decay curves were bimodal for all treatments and hence did not conform to a simple pool model. It is concluded that dietary safflower oil causes more rapid formation of cholate than does dietary beef tallow in the cholesterol-fed rat. The increase in cholate synthesis rate and decrease in cholate half-life suggest that polyunsaturated fat reduces cholesterol levels in plasma and liver of cholesterol-fed rats through the stimulation of cholesterol oxidation.

6499 THE ACUTE AND CHRONIC EFFECTS OF ETHANOL ADMINISTRATION ON BILE SECRETION IN THE RAT. *(E.)* Maddrey, W. C.; Boyer, J. L. (Yale Univ. Sch. Med., New Haven, Conn.). *J. Lab. Clin. Med.* 82(2):215-225, 1973.

Either a 25% solution of 95% ethanol or isocaloric glucose in drinking water was pair-fed with lab chow to 300 g male Sprague-Dawley rats for 2 weeks. These diets allowed 28.4% of calories as ethanol or glucose and sustained growth. After 2 weeks, bile secretory function was assessed. Liver and body weights were similar in the 2 pair-fed groups. When blood ethanol levels were negligible, bile flow and bile salt secretion were significantly increased in ethanol-fed animals. Bile-to-plasma ratios of ^{14}C-erythritol approximated 1.0 in both groups, and estimates of canalicular bile flow suggested that ethanol was stimulating a bile canalicular secretory mechanism. Ethanol significantly increased the nonbile salt-dependent fraction of bile, as indicated by comparison of regression lines of bile salt secretion vs. flow. The rate of bile salt secretion was also enhanced in ethanol-fed animals. Augmentation of the nonbile salt-dependent fraction of bileflow was not associated with an increase in the biliary excretion of hexuronic acids. In contrast, bile flow was depressed when blood levels of ethanol were elevated at the time of study or when ethanol was added acutely to the perfusate of normal isolated rat liver preparations. These findings suggest that ethanol inhibits or stimulates bile secretion depending on the blood alcohol level and duration of intake. It is also apparent that chronic ethanol feeding is associated with stimulation of the nonbile salt-dependent fraction of canilicular bile flow in the rat.

6500 SOLUBITILITY OF CHOLESTEROL IN BILE SALT-LECITHIN MODEL SYSTEMS. *(E.)* Tamesue, N.; Inoue, T.; Juniper, Jr., K. (Univ. Arkansas Med. Ctr., Little Rock). *Am. J. Dig. Dis.* 18(8):670-678, 1973.

Model systems of unconjugated and conjugated bile salts and lecithin at physiologic concentrations were used to study cholesterol solubition. Conjugated bile salts had slightly less dissolving power than unconjugated forms. Taurine conjugates showed less power than glycine conjugates. Lecithin increased the dissolving power of each bile salt proportionally up to a lecithin-bile salt molar ratio of 1.0, when the amount of cholesterol dissolved was triple that dissolved in the absence of lecithin. At most physiologic ratios of lecitin-bile salt, however, lecithin doubles the amount of cholesterol dissolved. Lecithin reduces significant differences in the cholesterol dissolving power of both unconjugated and conjugated bile salt species. Mixtures of unconjugated bile salts show additive effect in the absence of lecithin. When lecitin is present, the dissolving power of deoxycholate predominates over cholate, and that of cholate over chenodeoxycholate. Mixtures of conjugated bile salt species have an additive effect on dissolving power in both the presence and absence of lecithin. The cholesterol saturation curves for glycodeoxycholate and glycocholate at a total bile salt concentration of 150 mM, considered representative of the cholesterol dissolving power of human gallbladder bile, showed less dissolving power at lecithin-bile salt ratios of 0.25 to 0.50 than did previously determined curves. Current results show that changes in total bile salt concentration encountered in human gallbladder bile do produce significant shifts in the saturation curve.

6501 THE INTESTINE AS A SOURCE OF A PORTAL BLOOD FACTOR RESPONSIBLE FOR LIVER REGENERATION.

(E.) Fisher, B.; Szuch, P.; Levine, M.; Saffer, E.; Fisher, E. R. (Univ. Pittsburgh Sch. Med., Pa.). *Surg. Gynecol. Obstet.* 137(2): 210-214, 1973.

The effect of intestinal alterations on DNA synthesis in regenerating liver after partial hepatectomy or portacaval shunting was studied in single Lewis isogeneic female rats and in cross-circulated pairs of Buffalo rats. Test rats were injected in the femoral vein with ^{3}H methyl thymidine (10 C) 23 hr after partial hepatectomy or immediately after separation from cross circulation. DNA extracted from the livers of rats after sacrifice was assayed with a scintillation counter. While resection of a segment of jejunum or ileum impaired regeneration, the most profound inhibition of specific activity by the diphenylamine procedure; radioactivity was determined with a scintillation counter. While resection of a segment of jejunum or ileum impaired regeneration, the most profound inhibition of specific activity was effected by isolation of a 30 cm loop of the terminal part of the lieum. In cross circulation studies, the degree of DNA synthesis in the liver of the normal rat increased with the amount of liver resected in the partner. Addition of segmental resection of the small intestine to partial hepatectomy and portacaval shunt abolished the response in the liver of the intact partner. These findings suggest that the humoral factor responsible for liver regeneration does not arise in the hepatic remnant but is in portal blood. It is noted that folic acid, which is absorbed by the jejunum, participates in DNA synthesis if first reduced to tetrahydrofolic acid, and that vitamin B_{12} may facilitate this reduction. Removal or isolation of jejunum or ileum may result in elimination of one or the other of these agents from the portal blood, thus limiting the effectiveness of the other.

6502 OBSTRUCTIVE JAUNDICE LIPOPROTEIN PARTICLES STUDIED IN ULTRATHIN SECTIONS OF LIVERS OF BILE DUCT-LIGATED MICE.

(E.) Stein, O.; Alkan, M.; Stein, Y. (Hebrew Univ.-Hadassah Med. Sch., Jerusalem, Israel). *Lab. Invest.* 29(2):166-172.

The main bile duct was ligated in white female albino mice and their blood and livers were examined 48 to 96 hr later to study the origin of obstructive jaundice lipoprotein. In negatively stained preparations stacks of disk-like particles were seen in serum. Numerous bilayer profiles were visible in ultrathin sections of serum-gelatin blocks. Stacks of particles were found in the space of Disse. However, no structures resembling these particles were seen in the endoplasmic reticulum. the Golgi apparatus, or the cytoplasm of the hepatocytes. Endocytosis of the particles occurred both into coated vesicles of hepatocytes and into phagocytic vacuoles of Kupffer cells. These results suggest that even though the components of the obstructive jaundice lipoprotein originate in the liver, the formation of the disk-like particles occurs in the blood, and both Kupffer cells and hepatocytes apparently participate in the removal of the particles from the circulation.

6503 BILE ACID METABOLISM IN MAMMALS. V. STUDIES ON THE SEX DIFFERENCE IN THE RESPONSE OF THE ISOLATED PERFUSED RAT LIVER TO CHENODEOXYCHOLIC ACID.

(E.) Yousef, I. M.; Magnusson, R.; Price, V. M.; Fisher, M. M. (Dept. Med., Univ. Toronto, Ontario, Canada). *Can. J. Physiol. Pharmacol.* 51(6):418-423, 1973.

The hepatic metabolism of chenodeoxycholic acid (CDCA) was studied using isolated perfused livers from Wistar rats of both sexes. In 12 perfusions, 6 male and 5 female, 30 μmol of CDCA were added to the perfusion medium, and in 12 other perfusions, also 6 of each sex, 1 μmol of CDCA was added to the perfusion medium. CDCA was added after 2 hr of base-line perfusion and the bile acids of liver, plasma, and bile were analyzed by combined thin-layer and gas chromatography. In the 2 hr of perfusion prior to the addition of exogenous CDA, there were sex differences in the kinetics of bile acid secretion in the bile and in the bile acid composition of that bile. Following the addition of CDCA to the perfusion medium, the female liver was found to take up more CDCA from the perfusion medium to store more CDCA, and to convert less CDCA to β-muricholic acid. Toxicity of CDCA for the isolated perfused liver of the female rat is not due to α- or β-muricholic acid, the end products of

CDCA metabolism in the rat. The greater capacity of the male liver to convert potentially toxic CDCA to nontoxic β-muricholic acid partly explains the observed sex difference in CDCA hepatotoxicity.

6504 MECHANISM FOR THE CHOLERETIC ACTION OF OUABAIN. STUDIES OF BILE SECRETION FROM THE ISOLATED RAT LIVER. 2nd REPORT. *(Ger.)* Graf, J.; Korn, P.; Lindner, A.; Peterlik, M. (Inst. Gen. Exp. Pathol., Univ. Vienna, Austria). *Wien. Klin. Wochenschr.* 85(5):70-74, 1973.

Bile secretion was measured on isolated, perfused livers from male Wistar SPF rats before and after addition of ouabain (2.7 x $10^{-5}$to 2.1 x 10^{-3}M) to the perfusion medium. Ouabain increased bile secretion by 12-277% for 40-140 min. The increase in bile secretion and duration of bile secretion increased with increasing doses of ouabain. Most of the ouabain (89-96%) was rapidly taken up by the liver, but only 7.3-51% was excreted in the bile. Over a wide range of ouabain concentrations, ouabain excretion was independent of the dose added, but the time course and rate of bile flow did correlate with ouabain uptake by the liver. Ouabain uptake was accompanied by a loss of potassium and in increase in sodium in the liver, suggesting that membrane (Na^+-K^+) ATPase is inhibited at the sinusoidal membrane. The increase in Na^+ transport at the canalicular membrane of the liver cell is probably the cause of oubain-induced bile secretion.

6505 EFFECT OF SPIRONOLACTONE AND PREGNENOLONE-16α CARBONITRILE ON BILIRUBIN METABOLISM AND PLASMA LEVELS IN MALE AND FEMALE RATS. *(E.)* Radzialowski, F. M. (Searle Labs., Chicago, Ill.). *Biochem. Pharmacol.* 22(13):1607-1611, 1973.

The effect of spironolactone treatment (100 mg/kg/day) or pregnenolone-16α-carbonitrile treatment (40 mg/kg/day) on the activity of hepatic bilirubin glucuronyltransferase in 10,000 *g* supernatant fraction from male and female Charles River rats was studied. Bilirubin plasma levels were measured after 5 and 12 days of treatment with spironolactone or pregnelolone-16α-carbonitrile. Spironolactone significantly increased the rate of bilirubin conjugation in male and female rats after 5 days of treatment, from 3.37 to 4.56 and from 1.49 to 2.46 μg/mg protein/30 min, resp. Pregnenolone-16α-carbonitrile increased the rate of bilirubin conjugation from 3.37 to 4.35 in male and from 1.49 to 2.32 μg/mg protein/30 min in female rats. Plasma bilirubin levels were significantly reduced after 5 days of treatment with spironolactone in male rats. Both drugs caused significant decreases in plasma bilirubin levels in male and female rats after 12 days of treatment. These results suggest that spironolactone or pregnenolone-16α-carbonitrile may be useful in treating clinical hyperbilirubinemia where the excess bilirubin in the plasma is in unconjugated form.

6506 MEMBRANE PERMEABILITY OF HEPATIC MITOCHONDRIA AND LYSOSOMES STUDIED BY STRUCTURE-LINKED ENZYME CHANGES. *(E.)* Verity, M. A.; Brown, W. J. (Univ. California, Dept. Pathol., Los Angeles). *Exp. Mol. Pathol.* 19(1):1-14, 1973.

Mitochondrial and lysosome membrane permeability in adult Swiss albino male mice was studied in terms of changes in structure-linked enzyme activity. A linear correlation of particle light scattering and mitochondrial dehydrogenase activation was obtained as a function of Cu^{2+}-induced volume change. Mitochondrial dehydrogenase and lysosome hydrolase activities varied in accord with Boyle-van't Hoff's laws. This sugests that both particle systems behave as osmometers in potassium chloride solutions. The permeation rate of a solute into mitochondria or lysosomes was obtained from the rates of enzyme activation in isosmolar solute. Mitochondria and lysosomes were permeable to ammonium, acetate, and phosphate ions. Electron microscopy of mitochondrial pellets revealed mitochondrial changes consisting of a condensed → swollen conformation. Glycerol induced a loss of lysosome matrix but only partial lysosome destruction was seen after preincubation in ammonium phosphate. Such semiquantitative analyses of lysosome-vascuolar membrane permeability will aid in evaluating lysosome function in pathologic states.

6507 PHENOBARBITAL METABOLISM IN ETHANOL-INTOXICATED RATS. *(E.)* Coldwell, B. B.; Paul, C. J.; Thomas, B. H. (Drug Res. Labs., Dept. Natl. Health Welfare, Ottawa, Canada). *Can. J. Physiol. Pharmacol.* 51(6):458-463, 1973. **6507**

The effects of an acute dose of ethanol (3 g/kg) on the metabolism of ^{14}C-phenobarbital (50 mg/kg) was studied in male Wistar rats. Ethanol-treated rats had higher blood and tissue levels of radioactivity than control animals for 10-12 hr following oral administration of the drugs. No redistribution of radioactivity between blood and tissues was observed. No phenobarbital metabolites were found in the brain, and only traces of metabolites were detected in the blood and liver. Ethanol inhibited the excretion of radioactivity during the first 12 hr after dosing. This was due to reduced excretion of *p*-hydroxyphenobarbital. It is concluded that ethanol inhibits the hydroxylation of phenobarbital in the rat.

6508 THE ORIGIN OF LYSOLECITHIN IN HEPATIC BILE IN ACUTE CHOLECYSTITIS. AN EXPERIMENTAL STUDY ON RABBITS. *(E.)* Cahlin, E.; Gottfries, A.; Jonsson, J.; Schersten, T. (Surg. Clin. II, Univ. Goteborg, Sweden). *Acta Chir. Scand.* 139(4):372-376, 1973.

Acute cholecystitis was induced in rabbits by injection of sterile and chromatographically pure lysolecithin into the occluded and emptied gallbladder. At reoperation 48 hr later the concentration of lysolecithin had risen from 0.48 to 0.96 μg Pi/ml, while lecithin concentration decreased from 13.2 to 11.4 μg Pi/ml and that of bile acids from 12.9 to 11.4 μmol/ml. In a control series of rabbits, sterile 0.9% sodium chloride solution was injected into the occluded gallbladder. In another series of rabbits radioactive lysolecithin was injected into the occluded and emptied gallbladder and the specific radioactivity in lecithin and lysolecithin in the excreted hepatic bile was determined from 20 min to 48 hr after injection. The concentration of lecithin in hepatic bile was low during the first 3 hr (4.5 μgPi/ml), reaching control levels after 4 hr (12.1 μgPi/ml). Lysolecithin concentration was high the first hours (2.4 μgPi/ml), decreasing to 1.1 μgPi/ml after 4 hr. The results indicate that the increased concentration of lysolecithin in hepatic bile in acute cholecystitis is secondary to the cholecystitis, and that this increased concentration may be an effect of impairment of the liver function with decreased rate of acylation of lyso-intermediates in the synthesis of lecithin.

6509 DIURNAL VARIATION OF HEPATIC GLUTATHIONE CONCENTRATION AND ITS CORRELATION WITH 1,1-DICHLOROETHYLENE INHALATION TOXICITY IN RATS. *(E.)* Jaeger, R. J.; Conolly, R. B.; Murphy, S. D. (Harvard Sch. Public Health, Boston, Mass.). *Res. Commun. Chem. Pathol. Pharmacol.* 6(2):465-471, 1973.

Hepatic glutathione concentration was decreased in the livers of fasted male Holtzman rats. Liver glutathione had a diurnal rhythm in fed animals. The minimum glutathione concentration occurred between 7 p.m. and 1 a.m. The maximum hepatic glutathione concentration occurred between 7 a.m. and 1 p.m. Fasted animals with a decreased concentration of liver glutathione also had a diurnal variation, but it was greatly reduced in magnitude. Fed animals were more sensitive to the lethal and hepatotoxic effect of 1,1-dichlorethylene (2000 ppm) when exposed at periods of low hepatic glutathione concentration. Although there is no evidence of a time-dependent modification of 1,1-dichloroethylene toxicity in man, such a theory may explain some of the unaccountable injury from organic solvents which has in the past been ascribed to individual hypersensitivity.

6510 HAEMATOLOGICAL EFFECTS OF CHRONIC ETHANOL ADMINISTRATION AND FOLIC ACID DEFICIENCY IN MICE. *(E.)* Lockner, D.; Ericson, U. (Dept. Alcohol Res., Karolinska Inst., Stockholm, Sweden). *Acta Haematol. (Basel)* 49(4):242-253, 1973.

Experiments lasting from 5 weeks to 1 yr were conducted with male NMRI mice to investigate the anemia found in chronic alcoholics with liver damage. Different groups were given tap-water (controls), 10% alcohol, tap-water containing small amounts of methotrexate, or methotrexate plus 10% alcohol in tap-water. Alcohol or methotrexate (10 μg/day) alone caused no hematological changes. When both agents were combined, heavy anemia developed, indicating a synergistic effect of alcohol and folic acid deficiency. Only minimal changes could be observed in the livers of animals receiving alcohol or alcohol plus methotrexate, resp. That alcoholics developing anemia usually show liver damage does not contract these findings, as folic acid deficiency is caused both by the metabolic and social effects of prolonged heavy drinking. With increasing duration of abuse, the frequency of liver damage increases and may be concomitant but not necessarily causative to the development of anemia.

6511 EFFECT OF PHENOBARBITAL ON ACUTE TOXICITY AND LIVER DAMAGE INDUCED BY CERIUM CHLORIDE IN MALE MICE. *(E.)* Bjondahl, K.; Mottonen, M.; Nieminen, L. (Res. Ctr., Univ. Turku, Finland). *Ann. Med. Exp. Biol. Fenn.* 51(2):69-73, 1973.

Pretreatment with phenobarbital sodium in drinking water (0.05% solution) for 11 days significantly decreased the acute, lethal toxicity in male NMRI mice induced by cerium chloride (15 mg/kg, i.v.). Eleven days' phenobarbital pretreatment and 7 days' post-treatment also decreased this toxicity significantly and further decreased the amount of liver necrosis and fatty infiltration. When phenobarbital was given after the cerium injection and not before, there was no significant difference in mortality between test and control animals. Phenobarbital pretreatment does not increase secretion of cerium in bile. Therefore, the decrease in toxicity must result from the decreased severity of liver damage. Phenobarbital pretreatment increases the amount of smooth endoplasmic reticulum and accelerates drug metabolism, increasing the concentration of phospholipids and proteins, and thereby reducing the toxicity of cerium chloride.

6512 EFFECT OF EXCESSIVE INTAKE OF THREONINE ON LIVER LIPIDS IN GROWING RATS. *(E.)* Ghang, Y. O.; Miller, G. J.; Yokota, F. (Div. Biochem., Univ. Wyoming, Laramie). *Nutr. Rep. Int.* 8(3):187-193, 1973.

Threonine intake was studied in 24 weanling male Sprague-Dawley rats. When rats received a 6% casein diet, total liver lipids were increased and phospholipids reduced compared with rats given an 18% casein diet. Supplementation of 5% DL-threonine to the 6% casein diet or an increase in the protein level to 18% increased phospholipids and decreased liver lipid accumulation. Supplementation of 5% DL-threonine to the 18% casein diet caused no further change in either phospholipids or total lipids. The distribution of fatty acids in total liver lipids indicated that stearic acid and arachidonic acid concentrations were lower, and oleic and linoleic acid concentrations were higher in the low-casein group, as compared with rats on the high-casein diet. When the low-casein diet was supplemented with 5% DL-threonine, a fatty acid composition was produced which resembled that ound in rats on the high-casein diet. These findings suggest that the adverse effects of protein deiciency on lipid metabolism may be alleviated by upplementation with large amounts of threonine.

513 EFFECT OF HYPOTHERMIA ON CARBON TETRACHLORIDE-INDUCED CHANGES IN HEPATIC ULRASTRUCTURE. *(E.)* Kurstak, C.; Cote, M. G.; Plaa, . L. (Fac. Med., Univ. Montreal, Canada). *Toxiol. Appl. Pharmacol.* 26(1):14-28, 1973.

ale Sprague-Dawley rats were divided into 5 groups: ormal animals treated with the corn oil vehicle; ormal animals treated with carbon tetrachloride CCl$_4$) (0.5 mg/kg); animals whose spinal cord was evered at the level of T$_2$ and allowed to become ypothermic; animals whose spinal cord had been evered at the level of T$_2$ allowed to become hypohermic and treated with CCl$_4$ and animals which had een cordotomized, placed in an incubator to mainain normal body temperature and treated with CCl$_4$. he histologic and ultrastructural alterations in the iver 6, 12, and 24 hr after CCl$_4$ were evaluated. Corotomy, when associated with hypothermia, resulted in elayed CCl$_4$-induced histologic and ultrastructural hanges. The changes observed at 24 hr were more seere than those observed at 6. Therefore, it appears hat the development of the lesion is only retarded y this procedure and that the lesion could develop ore extensively at later time periods. Cordotomy n normothermic rats did not protect against CCl$_4$ hus demonstrating that the hypothermic component f cordotomy was the principal protective element n these experiments. However, if the hypothermic esponse is merely a delayed degenerative process, ther forms of treatment would be necessary to preent full development of the process.

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516 EXPERIMENTAL INVESTIGATION OF NEW THERAPEUTICAL PRINCIPLES IN THE SURGICAL TREATENT OF PORTAL HYPERTENSION. *(Ger.)* Kreuzer, W. 2nd Surg. Clin., Univ. Vienna, Austria). *Wien. lin. Wochenschr. (Suppl.)* 85(27/28):1-17, 1973.

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6519 THE DISTRIBUTION OF RIBOSOMES BETWEEN DIFFERENT FUNCTIONAL STATES IN LIVERS OF FED AND STARVED MICE. *(E.)* Norman, M.; Gamulin, S.; Clark, K. (King's Coll. Hosp. Med. Sch., London, England). *Biochem. J.* 134(2):387-398, 1973.

6520 EFFECT OF IRRADIATION ON AMINO ACID IN VITRO INCORPORATION IN THE COURSE OF LIVER REGENERATION. *(E.)* Tasheva, B.; Markov, G.; Tsanev, R. (Biochem. Res. Lab., Bulgarian Acad. Sci., Sofia). *Z. Naturforsch.* 28c(5-6):313-315, 1973.

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6537 THE EFFECT OF SALICYLATE ON THE BILIARY EXCRETION OF ^{14}C-BISHYDROXYCOUMARIN IN RAT. *(E.)* Buttar, H. S.; Coldwell, B. B.; Thomas, B. H. (Drug Res. Labs., Dept. Natl. Health Welfare, Ottawa, Canada). *Br. J. Pharmacol.* 48(2):278-287, 1973.

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See also, 6148, 6151, 6161, 6337, 6372, 6639, 6657, 6665, 6700, 6708, 7559, 7624, 7858.

SECRETION AND METABOLISM

Intestine

RESPONSE OF MESENTERIC VESSELS TO VASOACTIVE DRUGS FOLLOWING AUTOTRANSPLANTATION OF THE L INTESTINE. *(E.)* Zetin, M.; Rosenquist, C. J.; blood, H. W.; Kohatsu, S. (Coll. Med., Univ. fornia, Irvine). *Invest. Radiol.* 8(3):138-142, .

ographic studies were made of the celiac and rior mesenteric arteries in dogs that had under- autotransplantation of the small intestine. A p of 4 dogs was studied 6-8 months following the ical procedure, which included resection of the l intestine, mesentery, superior mesenteric ar- , and superior mesenteric vein. The appearance he intact celiac and resected superior mesenteric els was first observed by selective injection of mine iothalamate 60%. Subsequently, the phar- logic response of the arteries was evaluated ra- raphically by infusing isoproterenol and giving her contrast injection. Finally, propranolol epinephrine were infused and another injection ontrast material was made. Normal animals (2) out surgery were studied as controls. The su- r mesenteric and celiac arteries appeared nor- n all cases. No collateral circulation from eliac artery was identified. Both the intact c and resected superior mesenteric arteries nded as expected to vasoactive drugs, indicat- hat the surgical procedure did not permanently the response to these drugs.

6618 COMPARATIVE STUDIES OF THE OCCURRENCE AND LOCALIZATION OF CARCINOEMBRYONIC ANTIGEN (CEA) AND A PERCHLORIC-ACID SOLUBLE ANTIGEN OF NORMAL COLONIC MUCOSA IN CARCINOMAS AND POLYPS OF THE LARGE INTESTINE. *(Ger.)* Tappeiner, G.; Denk, H.; Eckerstorger, R.; Holzner, J. H. (Inst. Pathol. Anat., Univ. Vienna, Austria). *Virchows Arch. (Pathol. Inst.)* 360:129-140, 1973.

Indirect immunofluorescence was used to compare the occurrence and localization of a perchloric acid soluble antigen of normal colonic mucosa (NC) with those of carcinoembryonic antigen (CEA) in 42 carcinomas and 4 polyps of the large intestine. In contrast to CEA, which was found in carcinomas, regardless of their degree of differentiation, the occurrence of NC was correlated with the degree of tumor differentiation. In some instances NC was not found at all in highly differentiated carcinomas which contained CEA, but was present in large quantities in the cytoplasm of tumor cells which were morphologically similar to goblet cells. NC was also found as "lakes" between tumor cells in poorly differentiated, anaplastic carcinomas with a tendency to produce mucus. NC was present in mucus from all mucus-producing tumors regardless of their degree of differentiation. In polyps, NC was present in goblet cells while CEA was present in lumen-like parts of goblet in normal mucosa adjacent to the tumor and in benign polyps and those undergoing malignant degeneration. It is not known whether this CEA was produced by normal epithelial cells in the colon or whether it was secreted from the adjacent tumor. The presence of CEA in carcinomas of the large intestine, regardless of their degree of differentiation, suggests that all carcinomas of the large intestine produce CEA but only certain carcinomas secrete it.

6619 CORTICOSTEROID-DEPENDENT CYCLOHEXIMIDE-EVOKED INCREASE OF SUCRASE AND MALTASE IN THE JEJUNUM OF SUCKLING RATS. *(E.)* Koldovsky, O.; Jumawan, J.; Herbst, J. J.; Palmieri, M. (Children's Hosp., Philadelphia, Pa.). *Biochim. Biophys. Acta* 309(2):370-378, 1973.

In the jejunum of suckling Charles River rats, cycloheximide (20-60 μg/100 g), a posttranslational inhibitor of protein synthesis, evoked a precocious increase of sucrase and maltase activities 48 and 72 hr later. Sucrase activity was maximal at the 30 μg dose. Maltase increased further with the higher doses, but not significantly between 40 and 60 μg. Adrenalectomy completely prevented the cycloheximide-evoked increase of maltase activity and substantially blocked the evoked increase of sucrase activity. Simultaneous administration of cortisone acetate (0.5 mg/100 g) and cycloheximide (30 μg/100 g) to adrenalectomized suckling rats caused a significant increase in specific activities of both hydrolases, but the total activity was increased only in the case of sucrase. Cycloheximide (30 μg/100 g) when used with a large dose of cortisone acetate (2 mg/100 g) did not influence the cortisone-evoked increase, but it did cause a significant decrease in the total maltase activity. Actinomycin D (25 μg/100 g) did not inhibit the cycloheximide-evoked increase of sucrase and maltase; the cortisone acetate (1 mg/100 g) evoked increase was inhibited by actinomycin D. Increases in sucrase and maltase activities produced by cycloheximide may be due to stimulation of endogenous corticosteroid secretion by the adrenals, but other mechanisms are also possible.

6620 MUCOSAL HEMODYNAMICS IN THE SMALL INTESTINE OF THE CAT DURING REGIONAL SYMPATHETIC VASOCONSTRICTOR ACTIVATION. *(E.)* Svanvik, J. (Dept. Physiol., Univ. Goteborg, Sweden). *Acta Physiol. Scand.* 89(1):19-29, 1973.

An indicator-dilution technique was used for a separate quantitative determination of mucosal and villous plasma and RBC flows and volumes on chloralose-anesthetized cats during stimulation of nerves surrounding the superior mesenteric artery. Atropine (1-1.5 mg/kg i.v.) was administered to block concomitantly activated vagal cholinergic fibers to the intestine. RBC were monitored after intraarterial injection of ^{32}P-labeled RBC and plasma after intraarterial injection of ^{32}P- or ^{198}Au-labeled plasma colloids. After an initial, marked mucosal vasoconstriction, the villous plasma flow increased above control values with a concomitant decrease in intestinal venous outflow. Blood flow of the entire mucosal layer stabilized at values similar to control values. After nerve stimulation was stopped, total venous outflow and mucosal blood flow showed a hyperemic response while villous plasma flow remained unchanged. These results suggest that during regional sympathetic vasoconstrictor activation blood flow increases in the intestinal villi while flow in deeper regions of the mucosa decreases.

6621 POST-IRRADIATION ENZYME ACTIVITIES OF RAT SMALL INTESTINE: EFFECTS OF DOSE FRACTIONATION. *(E.)* Becciolini, A.; Castagnoli, P.; Arganini, L.; De Giuli, G. (Med. Sch., Univ. Florence, Italy). *Radiat. Res.* 55(2):291-303, 1973.

Fractionated irradiation of the rat's abdomen with 1200 r, given in 2 equal exposures, changed enzyme activities of the epithelial brush border (lactase, invertin, maltase, and leucineaminopeptidase) of the small intestinal villi. In animals sacrificed at different times after the second irradiation 3 phases of enzyme activities were noted: an initial phase where activities increased above those in controls; an intermediate phase where the activities were reduced; and the final phase of return to normal of enzyme activity. The fall and subsequent recovery occurred earlier for maltase and invertin than for lactase and leucineaminopeptidase. When the time interval between doses is 6-24 hr, alterations of enzyme activities are analogous to, or more extensive than, those found after a single irradiation. When the interval is 48-72 hr, the initial phase of increased activity is absent. If the time interval is greatly increased (5 days), the effect of fractionated doses is similar to that produced by a single 650 r dose. It is suggested that in epithelial cells still undifferentiated at the moment of the first irradiation, the ability to synthesize the enzymes is reduced or abolished during subsequent migration in the villus. In the case of fractionated exposures, the initial increase takes place either when cells which form the villus are already differentiated at the moment of the second irradiation, or when a complete reformation has already taken place between exposures. Moreover, the dissociation after irradiation of the behavior of lactase suggests that the processes linked with the syntheses of these molecules have different degrees of radiosensitivity and different repair potentials.

6622 PROTEIN DIGESTION IN HUMAN INTESTINE AS REFLECTED IN LUMINAL, MUCOSAL, AND PLASMA AMINO ACID CONCENTRATIONS AFTER MEALS. *(E.)* Adibi, S. A.; Mercer, D. W. (Montefiore Hosp., Pittsburgh, Pa.). *J. Clin. Invest.* 52(7):1586-1594, 1973.

Normal male volunteers (aged 19-24 yr) were intubated with aspiration tubes or a biopsy capsule was placed in the small intestine. The subjects were fed a test meal containing 50 g of purified bovine serum albumin which served as the model dietary protein. Electrophoretic analysis of intestinal fluids showed that for at least 4 hr the ingested albumin was detectable in jejunal and ileal fluids. No protein was detected in intestinal fluids when a protein-free meal was fed. After the protein-rich meal, total jejunal concentrations of free and peptide amino acids rose from 3.21 to 29.29, and 15.94 to 117.97 μmol/ml, resp. Similarly, total ileal concentrations of free and peptide amino acids rose from 5.45 to 19.74, and 13.59 to 65.39 μmol/ml, resp. However, concentrations of free and peptide amino acids in intestinal fluids did not increase after the protein-free meal. While intracellular concentrations of amino acids in the jejunal mucosa did not change significantly, plasma concentrations of each free amino acid were increased after the protein-rich meal and were either decreased or remained unchanged after the protein-free meal. The amino acid composition of the ingested protein was reflected in the increases in intraluminal and plasma concentrations of individual amino acids after the protein-rich meal. It is concluded that after the ingestion of a test meal containing protein within the usual range of dietary intake the exogenous protein is the principal source of the increased free and peptide amino acids in the contents of the jejunum and ileum and in the plasma; there are greater amounts of amino acids present as small peptides than in the free form in the intestinal lumen; and the ingested protein can be recovered as late as 4 hr both in the jejunum and in the ileum.

6623 EFFECT OF VITAMIN A DEFICIENCY IN RATS ON INTESTINAL LIPIDS INCORPORATION OF ACETATE--^{14}C AND PALMITIC ACID-1-^{14}C INTO LIPID COMPONENTS.

E.) Ponnappa, B. C.; Rama Rao, P. B. R. (Central ood Technol. Res. Inst., Mysore, India). *Environ. hysiol. Biochem.* 3(3):154-160, 1973.

he effect of vitamin A deficiency on the incorpora- ion of acetate-1-^{14}C and palmitic acid-1-^{14}C into he intestinal lipids was studied. Groups of weanling ale albino rats were maintained on a vitamin A de- icient diet along with control rats receiving a itamin A supplement. Rats at the acute stage of eficiency, when liver stores of vitamin A were less han 25-30 I.U./g, were used in these studies. Ace- ate-1-^{14}C and palmitic acid-1-^{14}C were injected i.p. nd the rats sacrificed after 24 hr. Vitamin A defi- iency resulted in a 35-70% decrease in the trigly- erides and a relative increase in the free fatty cids of intestines. Incorporation of acetate-1-^{14}C as essentially the same in triglycerides whereas it as higher in cholesterol, cholesterol ester, phospholi- ids and glycolipid components. In contrast, palmitic- -^{14}C was incorporated to a greater extent in all but he cholesterol ester component in the vitamin A de- icient group. Significant ^{14}C activity from pal- itic acid-1-^{14}C was associated with the free cho- esterol fraction in the vitamin A deficient group hereas no incorporation was observed in intestinal holesterol of normal rats. It is suggested that n vitamin A deficiency, the oxidation of higher fatty acids and the utilization of the "acetate" derived from palmitate for synthesis of cholesterol are enhanced.

6624 POSTPRANDIAL CONCENTRATIONS OF FREE AND CONJUGATED BILE ACIDS DOWN THE LENGTH OF THE NORMAL HUMAN SMALL INTESTINE.

(E.) Northfield, T. C.; McColl, I. (Guy's Hosp., London, England). *Gut* 14(7):513-518, 1973.

Small intestinal samples were obtained by intubation from multiple sites along the small intestine in 11 subjects (10 males and 1 female, aged 21-66 yr) with no known gastrointestinal disease eating a normal diet and at laparotomy in a further 3 subjects. Free (unconjugated) bile acids were consistently demonstrated in ileal samples, and occasionally in lower jejunal samples, by thin-layer chromatography, supplemented in some cases by gas/liquid chromatography and by infrared spectroscopy. The free bile acid concentration, measured enzymically following thin-layer chromatography, reached a maximum (1 mM) in the lower ileum, where it represented half the total bile acid concentration. Following ampicillin (500 mg, p.o. or by tube), the concentration of free bile acids decreased markedly, suggesting that they resulted from bacterial deconjugation. Simultaneously, the total bile acid concentration increased, suggesting impaired absorption due to the reduced concentration of the more rapidly absorbed free bile acids. These results indicate that free bile acids in lower jejunal and ileal samples is a normal finding, and cannot be taken as evidence of abnormal bacterial overgrowth. It is also suggested that bacterial deconjugation at these sites may contribute to the remarkable efficiency of bile salt reabsorption.

6625 PROPERTIES OF ADENYLATE CYCLASE IN MUCOSAL CELLS OF THE RABBIT ILEUM AND THE EFFECT OF CHOLERA TOXIN.

(E.) Sharp, G. W. G.; Hynie, S.; Ebel, H.; Parkinson, D. K.; Witkum, P. (Massachusetts Gen. Hosp., Boston). *Biochim. Biophys. Acta* 309(2):339-348, 1973.

The properties of adenylate cyclase in mucosal epithelial cells of rabbit ileum were studied under control conditions and after stimulation by cholera toxin. A 3-5-fold stimulation of enzyme activity occurred after treatment with cholera toxin. Optimal conditions for activity were attained with Mg^{2+} concentrations between 5 and 25 mM at a pH of 8.0-9.0. The reaction rate was linear for 25 min at protein concentrations of the homogenate up to 40 μg/50 μliters incubation mixture when an ATP regeneration system was employed. Mn^{2+} at 3×10^{-4} to 1×10^{-3} M could replace Mg^{2+} but was inhibitory at 5 mM. Ca^{2+} was inhibitory at all concentrations above 10^{-5} M. Michaelis-Menten curves were linear with regard to ATP concentrations under both sets of conditions, V was 28 pmol/mg protein/min for control and 90 pmol/mg protein/min for toxin-treated enzyme. K_m for both conditions were 4×10^{-4} M. No evidence of cooperativity in the stimulation of enzyme activity was detected. An analysis of experiments involving combinations of F^- and toxin and a study of pyrophosphate inhibition suggests the mechanisms of activation by F^- and cholera toxin are different. Isoproterenol at 10^{-5} M stimulated the control enzyme, while epinephrine (10^{-7}-10^{-5} M) and propranolol (10^{-7}-10^{-5} M) had no effect. In contrast, isoproterenol, epinephrine and propranolol inhibited the enzyme after stimulation by cholera toxin. It appears that cholera toxin is only effective when applied to the intact cell. After a short latent period, a progressive increase in enzyme activity occurs which may maximize 5 to 6 hr later. A similar pattern might be obtained if the toxin itself is an enzyme which gradually changes the inhibitory membrane environment of adenylate cyclase.

6626 EFFECT OF PENTAGASTRIN ON ADULT RAT DUODENAL CELLS IN CULTURE.

(E.) Lichtenberger, L.; Miller, L. R.; Erwin, D. N.; Johnson, L. R. (Univ. Oklahoma Helath Sci. Ctr., Oklahoma City). *Gastroenterology* 65(2):242-251, 1973.

Gastrin and its synthetic derivative, pentagastrin, trophically stimulate gastrointestinal tissue *in vivo*. The effect of the gastrointestinal hormone on an *in vitro* tissue culture system was studied. An adult rat duodenal culture line was established. Half the cultures were treated with pentagastrin (0.5 μg/ml/day) and the control cultures were treated with saline. After 3 months, the pentagastrin-treated cultures were ~90% epithelial cells and ~10% fibroblasts, whereas the control cultures constituted an epithelial-fibroblast admixture, ~50% of each. The epithelial cells were quite similar in structure to crypt epithelial cells, although positive identification could not be made. The pentagastrin-treated cultures had a faster doubling time, 19.5 hr, than controls, 31.5 hr. This was due in part to a greater percentage of proliferative cells in the hormone-treated cultures (73%) in comparison to the control cultures (36%). This latter measurement was performed by monitoring the nuclear incorporation of ^{3}H-thymidine. These results support the contention that gastrin trophically affects duodenal tissue by acting directly on the target epithelial cells.

6627 HEXOKINASE IN ISOLATED EPITHELIAL CELLS FROM RAT INTESTINE.

(E.) Jones, G. M.; Mayer, R. J. (Med. Sch., Univ. Nottingham, England). *Biochim. Biophys. Acta* 304(3):634-641, 1973.

Intact epithelial cells uncontaminated by lamina propria were obtained from male Wistar rats by vibration of everted intestine in isoosmotic ethylenediaminetetraacetic acid. The results of subcellular fractionation indicated that 13.5-15% of the hexokinase activity of homogenates of isolated cells was recovered in the particle free supernatant, and that the particulate hexokinase was bound to mitochondria. It could not be determined whether any hexokinase was bound to the brush border due to heavy contamination of the brush border fraction with mitochondria. Fractions having relatively high leucine aminopeptidase and alkaline phosphatase activities were low in hexokinase activity. Fractions having high succinate dehydrogenase activity contained most of the particulate hexokinase activity and had low leucine aminopeptidase and alkaline phosphatase activity. Only 29-32% of the total homogenate activity was present in the brush border plus nuclear fraction. The association of some small fraction of hexokinase with the brush border of epithelial cells cannot be ruled out, although hexokinase activity present in the brush border fraction may be due to mitochondrial contamination. Very little hexokinase activity is associated with fractions which are only enriched with the brush border markers, leucine aminopeptidase, and alkaline phosphatase.

6628 LIPID CONTENT OF THE RAT SMALL INTESTINAL MUCOSA AND SERUM, IN THE FASTING AND FED STATE.

(E.) Cotton, P. B. (St. Thomas' Hosp., London, England). *Digestion* 8(3):239-247, 1973.

The content of various lipid fractions was measured by thin-layer chromatography in suspensions of villus cells from the small intestinal mucosa of male Wistar rats. Rats were raised to a weight of 245-315 g on Spillers autoclave diet, consisting largely of triglycerides and free fatty acids. Fasted rats received only water for 48 hr. Other experiments were performed 120-180 min after placing a lipid emulsion (10 mg cholesterol, 5 mg cholesterol esters, 25 mg free fatty acids, 25 mg triglycerides, 18 mg phosphatidyl choline, 1 mg phosphatidyl ethanolamine) into the rats' stomachs. Scraping of the intestinal mucosa was far more effective than pronase digestion since results obtained by the latter method depended upon duration of exposure to pronase and the degree of agitation during digestion. The pronase method removed cells mainly from villus tips, whereas the scraping method denuded the entire villus. However, when mean lipid contents were compared for a standard DNA content, the results obtained by these 2 methods were quite similar except for the phosphatidyl choline fraction. After 120 and 150 min, mucosal samples from fed rats contained more than twice the mean lipid content of samples from fasted rats. In contrast to mucosal cells, serum contained larger amounts of cholesterol and almost no phosphatidyl ethanolamine. A comparison of fatty acids in the diet with those in mucosal cells of fasting rats showed striking differences in the neutral lipid fraction which made up most of the diet. These results indicate that villus mucosal cells contain sufficient lipid for exfoliation to constitute a significant potential source of lipid loss into the intestinal lumen.

6629 EFFECT OF SODIUM TAUROCHOLATE ON INTESTINAL LACTOSE HYDROLYSIS IN THE RAT. *(Ger.)*

ohmer, R.; Rommel, K. (Ctr. Internal Med. Pediatr.,
niv. Ulm, Germany). *Z. Gastroenterol.* 10(1):35-39,
972.

n male Wistar rats a solution containing 100 mg/100
l lactose and 8 x 10^{-3} M/liter sodium taurocholate
as perfused *in vivo* through a 10-cm long segment of
ntestine, beginning 30 cm distal to the pylorus, at
rate of 0.2 ml/min. Perfusion was carried out for
0 min, and the perfusion fluid was collected in 5
ractions, 10 min apart, starting after 10 min of
erfusion. Sodium taurocholate caused significant
nhibition of lactose hydrolysis and water absorp-
ion. In the presence of sodium taurocholate, 11.5%
f the lactose was hydrolyzed in the first 10 min and
.4% in the last 10 min of perfusion. When only
actose was present in the perfusion fluid, 34.5%
f the lactose was hydrolyzed in the first 10 min and
3.5% in the last 10 min. Thus, sodium taurocholate
educed lactose hydrolysis by about two-thirds. By
easuring polyvinylpyrrolidone concentrations, it was
ound that almost no water absorption occurred
etween the intestine and intestinal lumen in the
resence of sodium taurocholate. The concentrations
f free galactose in the perfusion fluid (0-3 mg/100
.) were within the limits of error for the method
ed in analyzing galactose so that it was impossible
make a statistical comparison.

30 ACTIVE SECRETION OF CALCIUM BY ADULT RAT ILEUM AND JEJUNUM IN VITRO. *(E.)*
lling, M. W.; Kimberg, D. V. (Harvard Med. Sch.,
ston, Mass.). *Am. J. Physiol.* 225(2):415-422,
73.

lcium was actively secreted from the serosal-to-
cosal surface of adult male Holtzman rat jejunum
d ileum, but not duodenum, when studied *in vitro.*
e ileal secretory process was not saturable over
range of calcium concentrations from 0.125-11.2
. However, there was inhibition of secretion by
gh concentrations of magnesium and strontium.
tabolic inhibitors (nitrogen gassing and 2 mM
doacetate) both abolished net secretion and in-
eased unidirectional calcium fluxes, the mucosal-
-serosal surface flux more so than the serosal-
-mucosal. Net calcium flux was not observed
ross the ileum of either growing or vitamin D-
ficient animals. While dietary calcium depri-
tion (2 weeks) increased calcium absorption by
th adult ileum and duodenum, the magnitude of
rosal-to-mucosal secretion flux was unchanged in both
ssues; net secretion persisted in the ileum
ile there was net absorption in the duodenum.
mparisons of *in vitro* secretion values with the
sults of balance studies suggest that this pro-
s is the source of the clinically observed en-
genous fecal calcium.

1 VASCULAR REACTIONS IN THE SMALL INTESTINE OF THE CAT DURING HEMORRHAGE. *(E.)* Hag-
nd, U. (Dept. Physiol., Univ. Goteborg, Sweden).
Acta Physiol. Scand. 89(1):129-141, 1973.

By means of a plethysmographic technique the reactions within the consecutive vascular sections of the cat small intestine during and after 2.5 hr hemorrhagic hypovolemia were studied. The cats were bled 20 or 35% of their total blood volume. The animals bled 35% were divided into a shock and a non-shock group determined by blood pressure prior to retransfusion. On bleeding, intestinal blood flow resistance increased moderately but during the latter half of hypovolemia, flow resistance decreased markedly in the shocked animals and did not normalize upon retransfusion. The capillary surface area available for exchange did not change during the hypovolemia except in the shocked cats where a small increase was recorded. Tissue volume decreased rapidly upon bleeding, due to venoconstriction, but late in the hypovolemia and after retransfusion a continuous tissue volume increase was often seen, partly due to a certain pooling of blood but mainly because of transcapillary transfer of fluid. Much of this fluid was found in the intestinal lumen at autopsy, which also revealed hemorrhagic lesions in the intestinal mucosa of most of the animals.

6632 CIRCADIAN RHYTHM OF ALKALINE PHOSPHATASE ACTIVITY IN THE GOLGI ZONE OF MOUSE DUODENAL ENTEROCYTES. *(E.)* Hugon, J. S.; Charuel, C.; Laurendeau, D. (Med. Ctr., Univ. Sherbrooke, Canada). *Histochemie* 35(3):263-272, 1973. 1973.

6633 THE CHEMISTRY OF INTRALUMINAL DIGESTION. *(E.)* Hofmann, A. F. (Mayo Clin., Rochester, Minn.). *Mayo Clin. Proc.* 48(9):617-619, 1973.

6634 SURFACE DIGESTION OF CARBOHYDRATES. *(E.)* Newcomer, A. D. (Mayo Clin., Rochester, Minn.). *Mayo Clin. Proc.* 48(9):620-623, 1973.

6635 REDOX POTENTIAL IN CAECAL CONTENTS OF THE RAT AND AZO REDUCTION OF SALICYL-AZO-SULPHAPYRIDINE. *(E.)* Schroder, H.; Johansson, A. K. (Dept. Zoophysiol., Univ. Uppsala, Sweden). *Xenobiotica* 3(4):233-246, 1973.

6636 INTERSPECIFIC VARIATION IN THE LEVELS OF INTESTINAL ALKALINE PHOSPHATASE, ADENOSINE TRIPHOSPHATASE AND DISACCHARIDASES. *(E.)* Hietanen, E. (Dept. Physiol., Univ. Turku, Finland). *Comp. Biochem. Physiol. (A)* 26(2):359-369, 1973.

6637 HYPOTHALAMIC-PITUITARY NEUROSECRETORY SYSTEM IN CATS AFTER REMOVAL AND ISOLATION OF THE DUODENUM. POSSIBLE EFFECT OF INTESTINAL HOR-

MONES ON THE HYPOTHALAMIC-PITUITARY NEUROSECRETORY SYSTEM. *(Rus.)* Skvortsova, N. B.; Polenov, A. L.; Ugolev, A. M. (I. P. Pavlov Inst. Physiol., Leningrad, USSR). *Dokl. Akad. Nauk SSSR* 211(1):252-255, 1973.

6638 REGULATION OF A β-CYTOTROPIC FACTOR IN THE DUODENAL MUCOSA OF THE RAT. *(Fr.)* Zermatten, A.; Felber, J. P. (Nestle Hosp., Lausanne, Switzerland). *Experientia* 29(6):749, 1973.

6639 GASTRIN DEGRADATION BY PARTICLE FREE SUPERNATANTS OF LIVER AND SMALL BOWEL HOMOGENATES OF THE RAT. *(E.)* Dette, G. A.; Seelig, H. P. (Westend Clin., Free Univ., Berlin, Germany). *Acta Hepatogastroenterol.* 20(1):248-253, 1973. 1973.

6640 ARGINASE ACTIVITY IN RAT SMALL INTESTINAL MUCOSA. *(E.)* Harri, M. P.; Hartiala, K. (Dept. Physiol. Univ., Turku, Finland). *Acta Physiol. Scand.* 89(1):126-128, 1973.

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6642 BOVINE INTESTINAL CALCIUM-BINDING PROTEINS. PURIFICATION AND SOME PROPERTIES. *(E.)* Fullmer, C. S.; Wasserman, R. H. (New York State Vet. Coll., Ithaca). *Biochim. Biophys. Acta* 317(1):172-186, 1973.

6643 THE CHARACTER OF RELATIVE DENSITY OF THE CHYME IN THE INITIAL PORTION OF THE SMALL INTESTINE IN DOGS. *(Rus.)* Begeka, A. D.; Groisman, S. D. (Res. Inst. Physiol., Kiev, USSR). *Biull. Eksp. Biol. Med.* 75(6):15-17, 1973.

6644 ENZYME ACTIVITY OF THE SMALL INTESTINAL MUCOSA IN GROWING RATS CHRONICALLY EXPOSED TO HIGH TEMPERATURES. *(Rus.)* Rakhimov, K.; Korotina, N. A. (Lab. Dig. Physiol., Uzbek Acad. Sci., Tashketn, USSR). *Biull. Eksp. Biol. Med.* 75(6):21-23, 1973.

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6646 EFFECT OF AN A' AQUEOUS EXTRACT OF SMALL INTESTINAL MUCOSA ON THE G-2 PHASE OF JEJUNAL PROLIFERATIVE CELLS IN MICE. *(E.)* Andersson, P. (Univ. Inst. Pathol. Anat., Copenhagen, Denmark). *Virchows Arch. [Zellpathol.]* 13(3):233-246, 1973.

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6648 EFFECTS OF NOREPINEPHRINE AND SYMPATHETIC STIMULATION ON EXTRACTION OF OXYGEN AND ^{86}Rb IN PERFUSED CANINE SMALL BOWEL. *(E.)* Shepherd, A. P.; Mailman, D.; Burks, T. F.; Granger, H. J. (Univ. Texas Med. Sch., Houston). *Circ. Res.* 33(2):166-174, 1973.

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6653 INTESTINAL LYMPH FLOW DURING EXPERIMENTAL PORTAL HYPERTENSION IN UNANAESTHETIZED RATS. *(Fr.)* Leymarios, J.; Roze, C.; Souchard, M.; Debray, C. (Bichat Hosp., Paris, France). *J. Physiol. (Paris)* 66(1):43-49, 1973.

6654 CHEMOTACTIC ACTIVITY OF INTESTINAL STRANGULATION OBSTRUCTION FLUID FROM GERMFREE AND CONVENTIONAL RATS. *(E.)* Trippestad, A.; Midtvedt, T. (Inst. Surg. Res., Oslo, Norway). *Acta Pathol. Microbiol. Scand. [B]* 81(2):227-232, 1973.

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6660 RELEASE OF SEROTONIN FROM THE SMALL INTESTINE FOLLOWING HYPOTENSION IN THE CAT. *(E.)* Fara, J.; Haglund, U. (Health Sci. Ctr., State Univ. New York, Stony Brook). *Eur. Surg. Res.* (2):152-161, 1973.

661 CHARACTERIZATION OF MEMBRANE ISOLATED FROM THE INTESTINAL BRUSH BORDER IN MAN. *(It.)* ndria, G.; de Masi, R. V.; Cecio, A. (Pediatr. lin., Univ. Naples, Italy). *Boll. Soc. Ital. iol. Sper.* 48(21):776-779, 1972.

662 CHANGES OF SOME COEFFICIENTS OF INTESTINAL CLEARANCE IN ACUTE UREMIA IN DOGS. *(E.)* dam, W.; Arasimowicz, C.; Manys, K.; Knapowski, J. Second Clin. Internal Dis., Poznan, Poland). *cta Physiol. Pol.* 23(2):263-270, 1972.

663 INTESTINAL DEFENCE IN THE YOUNG PIG - A REVIEW OF THE SECRETORY ANTIBODY SYSTEMS ND THEIR POSSIBLE ROLE IN ORAL IMMUNISATION. *(E.)* orter, P. (Unilever Res. Lab., Bedford, England). *et. Rec.* 92(25):658-664, 1973.

664 PROLIFERATION OF EPITHELIAL CELLS IN THE JEJUNAL CRYPTS OF ADRENALECTOMIZED AND DRENOCORTICAL HORMONE TREATED RATS. *(E.)* utton, P. J. M. (Dept. Anat., Monash Univ., Victoria, Australia). *Virchows Arch. [Zellpathol.]* 3(3):227-232, 1973.

6665 RATES OF CHOLESTEROL TURNOVER PROCESSES IN THE TRANSFER SPACE OF RAT. VI. INFLUENCE OF BILE DUCT LIGATION AND INGESTION OF BILE ACID OR CHOLESTYRAMINE. *(E.)* Lutton, C.; Mathe, D.; Chevallier, F. (Lab. Nutritional Physiol., Univ. Paris-Sud, Orsay, France). *Biochim. Biophys. Acta* 306(3):483-496, 1973.

6666 THE INTESTINE IS THE MAJOR SITE OF CHOLESTEROL SYNTHESIS IN THE RAT. *(E.)* Chevallier, F.; Lutton, C. (Lab. Nutritional Physiol., Univ. Paris-Sud, Orsay, France). *Nature* [*New Biol.*] 242(115):61-62, 1973.

6667 IN VITRO INDUCTION OF DRUG MONOOXYGENASE ACTIVITY BY PHENOBARBITAL IN THE ISOLATED MOUSE JEJUNUM. *(E.)* Scharf, R.; Ullrich, V. (Dept. Theoretical Med., Univ. Saarland, Homburg, Germany). *Naunyn Schmiedebergs Arch. Pharmakol.* 278(3):329-332, 1973.

6668 CHANGES IN ALDOLASE ISOZYMES OF THE DIGESTIVE TRACT DURING POSTNATAL DEVELOPMENT. *(E.)* Kawachi, T.; Tanaka, N.; Kogure, K.; Sugimura, T. (Natl. Cancer Ctr. Res. Inst., Tokyo, Japan). *Biochim. Biophys. Acta* 320:59-63, 1973.

6669 ENZYMATIC SYNTHESIS OF PLASMALOGENS. CHARACTERIZATION OF THE 1-*O*-ALKYL-2-ACYL-*sn*-GLYCERO-3-PHOSPHORYLETHANOLAMINE DESATURASE FROM MUCOSA OF HAMSTER SMALL INTESTINE. *(E.)* Paltauf, F.; Holasek, A. (Inst. Biochem. Med., Univ. Graz, Austria). *J. Biol. Chem.* 248(5):1609-1615, 1973.

6670 EFFECT OF AMPHOTERICIN B ON SODIUM AND WATER MOVEMENT ACROSS NORMAL AND CHOLERA TOXIN-CHALLENGED CANINE JEJUNUM. *(E.)* Chen, L. C.; Guerrant, R. L.; Rohde, J. E.; Casper, A. G. T. (Cholera Res. Lab., Dacca, Bangladesh). *Gastroenterology* 65(2):252-258, 1973.

See also, 6153, 6214, 6257, 6276, 6288, 6291, 6302, 6307, 6349, 6351, 6390, 6401, 6406, 6684, 7316, 7483, 7486.

6671 EFFECTS OF INTRA-ARTERIAL PHENTOLAMINE IN EXPERIMENTAL INTESTINAL ISCHAEMIA IN THE RABBIT. *(E.)* Guy, J. M.; Davis, R. L.; McLachlan, M. S. F.; Evans, K. T. (Welsh Natl. Sch. Med., Cardiff, Wales). *Br. J. Radiol.* 46(546):440-445, 1973.

A loop of ileum on its mesentery was withdrawn from the abdomen of the anaesthetized rabbit and kept warm and moist. This induced intestinal ischemia, as judged by the external appearances of the bowel and by superior mesenteric angiography in 32 out of 52 animals. Ischemia was treated by infusing phentolamine into the superior mesenteric artery. Large doses (2 mg/kg) consistently produced marked improvement in angiographic and naked eye appearances. Smaller doses (0.2 mg and 0.02 mg/kg) were less consistently effective. In 16 of 17 animals receiving phentolamine, a vasodilation occurred. This was complete in all 7 of those receiving the higher dose, and in 6 of the 10 receiving the lower doses. Vasodilation persisted for 30-120 min. Phentolamine consistently produced a fall in blood pressure which was dose dependent and persistent. Death occurred within 1 hr of phentolamine infusion in 6 animals. It is concluded that treatment of intestinal ischemia by infusion of phentolamine into the superior mesenteric artery is unsafe.

6672 THERAPEUTIC IMPLICATIONS OF THE INTESTINAL MICROFLORA. *(E.)* Goldman, P. (Longwood Area Hosp., Boston, Mass.). *N. Engl. J. Med.* 289(12):623-628, 1973.

Intestinal flora seem to have an important role in the metabolism of salicylazosulfapyridine as they apparently reduce the azo bond in the compound. Since the compound is broken down by the flora at the site of its therapeutic effect, it has been suggested that the metabolites of the drug rather than the parent compound might be responsible for its effectiveness. When salicylazosulfapyridine (2 or 3 g, single dose) was given to normal volunteers, a small amount of the drug was found in the feces. Of the 2 metabolites of the drug, 5-aminosalicylate was found in high levels in the feces and sulfapyridine was found primarily in the urine. These results, which were obtained regardless of the route of administration, indicate that 5-aminosalicylate may indeed be responsible for the beneficial effects of the parent drug on the colon. Other transformations by the flora that may have therapeutic implications include the formation or elimination of potentially toxic compounds such as ammonia or urea. It is stressed that the biological activities of microflora must be studied as they exist within the host. It is suggested that this currently poorly understood area might be studied by an analysis of transformation of small molecules by the flora.

6673 APPLICATION OF THE PRINCIPLE OF INDICATOR DILUTION CURVES TO THE STUDY OF THE PORTAL FRACTION OF TOTAL LIVER BLOOD FLOW. *(Fr.)* Huet, P. M.; Lavoie, P.; Viallet, A. (Saint Luc Hosp., Montreal, Canada). *Union Med. Can.* 101(4):656-665, 1972.

Portal and total hepatic flow were measured in dogs by using indicator dilution curves. Uniform mixing of indocyanine green or RBC labeled with ^{51}Cr was obtained in the portal vein and intrahepatic circulation by injecting the indicator into the superior mesenteric artery. The difference between paired total hepatic blood flows obtained simultaneously from the two main hepatic veins ranged from 1.7 to 15.7% (mean 7.23%) with indocyanine green and from 1.2 to 26% (mean 8/08%) with labeled RBC. In 13 dogs a positive correlation was found between flows measured simultaneously with labeled RBC and the indicator dilution curves and those measured with electromagnetic flowmeters. It is suggested that indicator dilutions curves can be used for simultaneous determination of portal and total hepatic blood flow in cirrhotics with combined umbilico-portal and hepatic vein catheterization. The ratio between simultaneous flows is reliable, even with extrahepatic shunts, since the same rapidly injected indicator is analyzed in the portal vein and in the hepatic vein.

6674 PROTECTIVE EFFECTS OF AZATHIOPRINE AND PHENOBARBITAL ON ACUTE LIVER DAMAGE PRODUCED BY GALACTOSAMINE. *(E.)* Perings, E.; Brunner, G.; Vido, I.; Soling, H. D.; Creutzfeldt, W. (Med. Clin., Univ. Gottingen, Germany). *Acta Hepato-gastroenterol. (Stuttg.)* 20(2):130-134, 1973.

Administration of phenobarbital (50 mg/kg/day p.o. for 8 days) or azathioprine (25 mg/kg/day p.o. for 5 days) had a protective effective effect in hepatitis induced by galactosamine (500 mg/kg i.p.) in male Wistar rats. Both agents decreased the mortality, significantly inhibited increases in SGOT and SGPT activities, and significantly lowered the necrosis index in rats given galactosamine. Administration of azathioprine (25 mg/kg/day p.o. for 8 days) alone increased microsomal enzyme activity in the liver, but not to as great an extent as did phenobarbital (50 mg/kg/day p.o. for 8 days) alone. Galactosamine (500 mg/kg i.p.) alone significantly decreased cytochrome P-450 activity but had no effect on the activities of reduced nicotinamide adenine dinucleotide phosphate (NADPH)-cytochrome c reductase or uridine diphosphate (UDP)-glucuronic acid transferase. When administered with galactosamine, a significant decrease occurred in the effect of phenobarbital on microsomal enzymes. Cytochrome P-450 and NADPH-cytochrome c reductase activities were higher than in galactosamine-treated rats, while UDP-glucuronic acid transferase activity had decreased almost to the levels in rats with galactosamine hepatitis. In contrast, galactosamine almost completely abolished the effect of azathioprine; only cytochrome P-450 activity remained significantly higher than in rats treated with galactosamine alone. These findings suggest that increased activities of cytochrome P-450 or some other microsomal factors are involved in the protective action of azathioprine and phenobarbital in galactosamine hepatitis.

6675 THE SMALL INTESTINE IN HYPOTENSION AND HEMORRHAGE. AN EXPERIMENTAL CARDIOVASCULAR STUDY IN THE CAT. *(E.)* Haglund, U. (Dept. Physiol., Univ. Goteborg, Sweden). *Acta Physiol. Scand.* [suppl.] (387):1-37, 1973.

The series-coupled vascular sections of the cat small intestine were studied by a plethysmographic technique in simulated hemorrhagic shock resulting from a 2.5 hr hemorrhage, amounting to 30-40% of the blood volume. The resistance vessels constricted on bleeding. On retransfusion resistance vessel tone remained below control. The precapillary sphincters relaxed on bleeding. After retransfusion their tone normalized. The intestinal capacitance vessels rapidly constricted on bleeding. A dilatation of the capacitance vessels was observed during prolonged hemorrhagic hypovolemia. The increase of regional blood volume amounted to half the reduction seen on bleeding. Augmentation of tissue volume, beyond that caused by the dilatation of the capacitance vessels, was observed during the late half of hypovolemia. Hemorrhagic lesions in the small intestinal mucosa, localized in the villous tips, were seen after reduced intestinal blood flow. Small amounts of oxygen, supplied *via* an intraluminal perfusion of oxygenated saline, prevented these lesion. Nitrogenated saline did not, suggesting that tissue hypoxia, but not the luminal contents, is the key factor in the pathogenesis of the mucosal lesions. A depressing effect on the heart occurred during simulated shock. This cardiodepressant effect was prevented if intestinal venous blood was collected during the first 4-5 min after the hypotension and substituted with blood from a healthy donor animal. A causal relation bewteen the hemorrhagic mucosal lesions and the intestinal release of cardiotoxic material is suspected. The material may be products of the mucosal tissue destruction.

6676 EXPERIMENTAL STUDIES ON THE PATHOPHYSIOLOGICAL CONSEQUENCES OF MESENTERIC STENOSIS ON THE STOMACH. *(Ger.)* Funovics, J.; Kretschmer, G.; Piza, F.; Pregel, I.; Zekert, F. (1st Surg. Clin., Univ. Vienna, Austria). *Langenbecks Arch. Chir.* 333(1):29-38, 1973.

The effect of changes in blood flow in the superior mesenteric artery on celiac and gastric blood flow, gastric acid secretion, and gastric morphology was studied in anesthetized dogs in which the pylorus had been ligated to prevent duodenal reflux and loss of acid. Stenosis of the superior mesenteric artery with a 53% decrease in blood flow significantly increased celiac blood flow from 380 to 440 ml/min and blood flow in the inferior mesenteric artery. After 60 min acid secretion had increased linearly to 4 times the mean initial value; this increase was highly significant. Occlusion of the superior mesenteric artery for 30 min increased celiac and inferior mesenteric blood flow to about 1.5 times their initial values. Erosions of the gastric mucosa were found in 1 dog and single or multiple ulcers in 3 of the 5 dogs. After stenosis of the superior mesenteric artery for 4 hr with a reduction of blood flow to 47% of its initial value and the gastroduodenal artery open, celiac flow increased significantly from 187 to 232 ml/min, as did blood flow in the left gastric artery; acid secretion increased to 2.5 times the initial level. With stenosis of the superior mesenteric artery and closure of the gastroduodenal artery no significant change occurred in mesenteric or gastric blood flow or in acid secretion. Of the 6 dogs in this group, 3 developed gastric erosions and 1, a single ulcer; no multiple ulcers were found. These findings suggest that decreases in blood flow through the superior mesenteric artery may be implicated in the pathogenesis of gastric ulcers.

6677 QUANTITATIVE AND QUALITATIVE CHANGES IN THE FECAL FLORA OF RATS FED A HIGH LIPID DIET. *(It.)* Minelli Bertazzoni, E. (Inst. Pharmacol., Univ. Padua, Verona, Italy). *Boll. Soc. Ital. Biol. Sper.* 48(21):730-733, 1972.

Fecal lipid contents and fecal flora were studied in female Wistar rats fed a high-lipid, high-sugar, low-protein diet (Handler's diet) and those fed a standard diet for 21 days. The total lipid content of the feces was 183.593 ± 0.537 mg/100 g dry weight in rats fed Handler's diet and 23.163 ± 0.118 mg/100 g dry weight for the controls. The total number of aerobic bacteria, particularly of coliform bacteria and lactobacilli, was almost 3 times higher in rats fed Handler's diet than in controls fed standard diet. Smaller increases occurred in noncoliform enterobacteria and streptococci, while the number of *Salmonella*, sulfur-producing enterobacteria, and fungi remained unchanged. This increase in fecal flora is considered to result from steatorrhea, rather than *vice versa*.

6678 THE EFFECT OF ANTIGEN DEPRIVATION ON THYMUS-DEPENDENT AND THYMUS-INDEPENDENT LYMPHOCYTES IN THE SMALL INTESTINE OF THE MOUSE. *(E.)* Ferguson, A.; Parrott, D. M. V. (Dept. Bacteriol., Univ. Glasgow, Scotland). *Clin. Exp. Immunol.* 12(4): 477-488, 1972.

In spite of the lack of intraluminal antigenic stimulation, isografts of fetal small intestine implanted under the kidney capsules of adult syngeneic CBA and BALB/c mice grew normally and contained thymus-dependent and independent lymphocytes. In these grafts the Peyer's patches are very small, lack germinal centers and have small thymus-dependent areas. Intraepithelial lymphocyte counts were made in normally sited small intestine of immunologically intact and thymus-deprived mice, in grafts implanted in intact and thymus-deprived mice, and in a group of neonatally thymectomized and control mice. A significant depletion of intraepithelial lymphocytes was noted in neonatally thymectomized mice, and a great reduction in numbers of intraepithelial lymphocytes in grafts, deprived of antigen, when compared with normally sited intestine of the same age. These results indicate that in the mature small intestine, whether or not exposed to antigen, the majority of lymphocytes in the Peyer's patch aggregates and scattered between the epithelial cells, are thymus-independent, B lymphocytes. It is suggested that in the adult, immune responses to most commensal gut antigens are likely to be thymus-independent.

6679 THE EFFECT OF FREQUENCY OF FEEDING ON THE FLOW AND COMPOSITION OF DUODENAL DIGESTA IN SHEEP GIVEN STRAW-BASED DIETS. *(E.)* Thompson, F. (Univ. Nottingham Sch. Agr., Leics, England). *Br. J. Nutr.* 30(1):87-94, 1973.

6680 THE INTERACTION OF BILIRUBIN WITH HUMAN SERUM ALBUMIN. *(E.)* Beaven, G. H.; Albis, A.; Gratzer, W. B. (Natl. Inst. Med. Res., London, England). *Eur. J. Biochem.* 33(3):500-510, 1973.

6681 ON THE FORMATION OF BILIVERDIN DURING PHOTOOXYGENATION OF BILIRUBIN IN VITRO. *(E.)* Lightner, D. A.; Crandall, D. C.; Gertler, S.; Quistad, G. B. (Dept. Chem., Texas Tech Univ., Lubbock). *F.E.B.S. Lett.* 30(3):309-312, 1973.

6682 TRIPEPTIDE IN HUMAN SERUM WHICH PROLONGS SURVIVAL OF NORMAL LIVER CELLS AND STIMULATES GROWTH IN NEOPLASTIC LIVER. *(E.)* Pickart, L.; Thaler, M. M. (Dept. Pediatr., Univ. California, San Francisco). *Nature* [*New Biol.*] 243(124):85-87, 1973.

6683 INHIBITORY EFFECT OF POTENT INTERFERON PREPARATIONS ON THE REGENERATION OF MOUSE LIVER AFTER PARTIAL HEPATECTOMY. *(E.)* Frayssinet, C.; Gresser, I.; Tovey, M.; Lindahl, P. (Sci. Res. Inst. Cancer, Villejuif, France). *Nature* 245(5421):146-147, 1973.

6684 FECAL FLORA IN MAN. I. COMPOSITION OF FECAL FLORA IN DIFFERENT AGE GROUPS. *(Ger.)* Mitsuoka, T.; Hayakawa, K. (Inst. Phys. Chem. Res., Wako-shi, Japan). *Zentralbl. Bakteriol. (Orig. A)* 223(3):333-342, 1973.

6685 THE PROBABLE REGULATION OF SOME ENZYMES IN THE PENTOSE PHOSPHATE SHUNT FOR DIETARY AMINO ACIDS. I. RELATION BETWEEN GLUCOSE-6-PHOSPHATE DEHYDROGENASE AND DIETETARY PROTEINS. *(It.)* Livrea, G.; Carrozza, G.; Giurgianni, C.; Manasseri, L.; Zimbaro, G. (Inst. Human Physiol., Univ. Messina, Italy). *Boll. Soc. Ital. Biol. Sper.* 48(21):696-699, 1972.

6686 MUCOUS AND SEROUS COMPONENTS OF THE SUBMANDIBULAR AND SUBLINGUAL GLANDS OF MACACA IRUS AND CERCOPITHECUS AETHIOPS. *(E.)* Jacobsen, N.; Hjalmar From, S. (Dept. Microbiol., Univ. Oslo, Norway). *Acta Histochem.* 46(2):281-287, 1973.

6687 A METHOD OF TRANSLATING ESOPHAGEAL PRESSURE TRACINGS INTO DIGITAL DATA FOR COMPUTER EVALUATION. *(E.)* Fox, J. E.; Beck, I. T.; (Hotel Dieu Hosp., Kngston, Canada). *Am. J. Dig. Dis.* 18(9):757-766, 1973.

6688 METAL COMPLEXES OF BILIRUBIN IN APROTIC SOLVENTS. *(E.)* Hutchinson, D. W.; Johnson, B.; Knell, A. J. (Dept. Molecular Sci., Univ. Warwick, Coventry, England). *Biochem. J.* 133(2):399-400, 1973.

6689 STUDY OF THE GASTROINTESTINAL IRRADIATION SYNDROME IN PIGS. *(Fr.)* Daburon, F.; Remy, J.; Nizza, P. (Lab. Appl. Radiobiol., Dept. Safety, Comm. Atomic Energy, Jouy-en-Josas, France). *Strahlentherapie* 144(3):343-361, 1972.

6690 PRESERVATION OF STRUCTURE AND FUNCTION IN CANINE SMALL INTESTINAL AUTOGRAFTS AFTER FREEZING. *(E.)* LaRossa, D.; Hamilton, R.; Ketterer, F.; Lehr, H. B. (Univ. Pennsylvania Hosp., Philadelphia). *Plast. Reconstr. Surg.* 52(2):174-177, 1973.

6691 ORTHOTOPIC LIVER TRANSPLANTS IN THE PIG: STUDY OF 25 PRELIMINARY CASES. *(Sp.)* Camprodon, R.; Jornet, J.; Salva, J. A.; Guerrero, J. A.; Pineiro, H.; Mendoza, C. G.; Miralles, J. A.; Kanarek, B. (Francisco Franco Munic. Sanit., Barcelona, Spain). *Rev. Esp. Enferm. Apar. Dig.* 40(2):115-126, 1973.

6692 INFLUENCE OF A GASTRIC TUBE ON SALIVARY AND PHARYNGEAL MUCOUS SECRETIONS IN MAN. *(E.)* Lambert, R.; Andre, C.; Descos, F.; Mbendi, S.; Andre, F. (E. Herriot Hosp., Lyon, France). *Digestion* 8(3):227-238, 1973.

6693 ROLE OF OSMOLALITY IN THE REGULATION OF THE GASTRIC BLOOD FLOW. *(Sp.)* Chacin, J.; Colina, J.; Diaz, P. (Fac. Med. Univ. Zulia, Maracaibo, Venezuela). *Acta Physiol. Lat. Am.* 22(1):15-25, 1972.

6694 β-GLUCOSIDASE AND LACTASE IN THE INTESTINE OF VERTEBRATES. *(Ger.)* Gossrau, R.

(Inst. Anat., Univ. Wurzburg, Germany). *Histochemie* 35(2):143-151, 1973.

6695 PROPERTIES OF HUMAN INTESTINAL GLUCOAMYLASE. *(E.)* Kelly, J. J.; Alpers, D. H. (Washington Univ. Sch. Med., St. Louis, Mo.). *Biochim. Biophys. Acta* 315(1):113-122, 1973.

6696 IDENTIFICATION OF INSULIN SYNTHESIZING POLYSOMES IN ISOLATED ISLETS OF LANGERHANS FROM RAT PANCREAS. *(E.)* Tjioe, T. O.; Kroon, A. M. (Lab. Physiol. Chem., State Univ., Groningen, Netherlands). *F.E.B.S. Lett.* 33(2):225-228, 1973.

6697 INTRA AND POSTOPERATIVE STUDY OF CLOTTING FACTORS IN EXPERIMENTAL AND CLINICAL LIVER TRANSPLANTATION. *(E.)* Monteiro Da Cunha, J. E.; Lima Goncalves, E.; Bevilacqua, R. G.; Machado, M. C. C.; Margarido, N. F. (Dept. Surg., Univ. Sao Paulo, Brazil). *Chir. Gastroenterol.* 6(1):3-13, 1972.

6698 EFFECT OF HISTAMINE ON THE INTRAGASTRIC TEMPERATURE AND BLOOD FLOW IN THE GASTRIC MUCOSA. *(Rus.)* Malov, Y. S. (no affil.). *Vrach. Delo* 4:22-25, 1973.

6699 EXPERIMENTAL INVESTIGATIONS OF NORMOTHERMIC ISCHEMIA TOLERANCE OF THE LIVER FOR THE PURPOSE OF GLUING LIVER LESIONS AFTER TOTAL INTERRUPTION OF LIVER CIRCULATION. *(Ger.)* Meissner, K. (Provincial Hosp., Salzburg, Austria). *Langenbecks Arch. Chir.* 33(1):39-46, 1973.

6700 SUCCESSFUL 24-HOUR PRESERVATION OF THE CANINE LIVER. *(E.)* Petrie, C. R.; Woods, J. E. (Mayo Clin., Rochester, Minn.). *Arch. Surg.* 107(3):461-464, 1973.

6701 THE PROLIFERATIVE RESPONSE AFTER PARTIAL HEPATECTOMY IN HYPOPHYSECTOMIZED RATS BEARING PROTACAVAL ANASTOMOSES. *(E.)* Weinbren, K.; Washington, S.; Dowling, F. (Dept. Pathol., Nottingham Univ., England). *Br. J. Exp. Pathol.* 54(4):429-436, 1973.

6702 EXPERIMENTAL ESOPHAGEAL LYE BURNS. II. CORRECTING ESTABLISHED STRICTURES WITH BETA-AMINOPROPIONITRILE AND BOUGIENAGE. *(E.)* Madden, J. W.; Davis, W. M.; Butler, II, C.; Peacock, Jr., E. E. (Univ. Arizona, Coll. Med., Tucson). *Ann. Surg.* 178(3):277-284, 1973.

6703 REVASCULARIZATION OF THE LIVER BY SPLENIC ARTERY IMPLANTATION. *(E.)* Kreuzer, W.; Moritz, E.; Wense, G.; Schenk, Jr., W. G. (Surg. Clin., Univ. Vienna, Austria). *Chir. Gastroenterol.* 7(1):51-60, 1973.

See also, 6617, 6620, 7204, 7745.

DIAGNOSTIC PROCEDURES

6704 SONOGRAPHIC DEMONSTRATION OF PANCREATIC NECROSIS: ULTRASOUND TOMOGRAPHY OF THE PANCREATIC REGION. *(Ger.)* Blauenstein, U. W.; Burger, J. (Med. Clin., Univ. Basel, Switzerland). *Dtsch. Med. Wochenschr.* 98(9):429-433, 1973.

Autopsy findings are compared with information obtained on ultrasonic tomograms made 7 and 13 days after the onset of symptoms of pancreatic necrosis in a 77-yr-old woman. Autopsy revealed extensive acute pancreatic necrosis, chornic pancreatitis, diffuse serofibrinous peritonitis, mesenteric thrombosis, and bilirubin and calcium carbonate stones in the gallbladder and bile ducts. Necrosis was also found in retroperitoneal adipose tissue, the mesentery, the left of the diaphragm, the greater omentum, and subcutaneous adipose tissue on the abdominal wall. Depending on the extent of lysis or tissue disintegration and suppuration, necrotic tissue appeared to be somewhat more homogeneous than intact tissue. This was particularly true for adipose and pancreatic tissue where negative contrast appeared in place of the original mosaic-like echo pattern in the advanced stages. Gallstones did not have large enough reflecting surfaces to show up on ultrasonic tomograms, although the stones were found to be the size of a pea at autopsy. In a 63-yr-old man with a confirmed diagnosis of pancreatic fibrosis, fibrotic changes were manifested as areas of negative contrast because of their relatively great acoustic homogeneity. The liver appeared to be greatly enlarged, and the very characteristic fine echo pattern of the hepatic parenchyma was not well defined due to cirrhosis.

6705 UMBILICAL VEIN PORTOHEPATOGRAPHY IN HEPATIC TRAUMA. *(E.)* Hankins, J. R.; Ayella, R. J.; Gill, W.; Cowley, R. A. (Univ. Maryland Hosp., Baltimore). *Surg. Gynecol. Obstet.* 137(2): 200-204, 1973.

Umbilical vein cannulation and portography, which can be performed through a small epigastric incision under local anesthesia or during laparotomy, have proved useful in the evaluation and management of a series of 14 patients (12 males and 2 females; aged 9-63 yr) with both blunt and penetrating hepatic trauma. The portogram showed the liver to be damaged in 8 of these 14 patients. Death occurred twice in this series, due to fat embolism (1) and coagulopathy (1). As a base line parameter, this method is invaluable in the early detection of delayed hepatic abscess formation. The introduction of the catheter at operation does not significantly prolong the operating time. The catheter can be left *in situ* up to 1 month postoperatively, so that repeated portograms may be obtained. The quality of visualization of the portal vein and its branches and of the hepatic parenchyma during the hepatogram phase is superior to that provided by other methods of roentgenographic visualization of the liver. This is accomplished with negligible risk and discomfort to the patients.

6706 THE IMPORTANCE OF THE ORAL d-XYLOSE TEST FOR DIAGNOSIS AND FOLLOW-UP IN CELIAC DISEASE. A COMPARISON BETWEEN SMALL BOWEL MORPHOLOGY AND d-XYLOSE TESTS. *(Ger.)* Harms, K. (Children's Clin., Univ. Munich, Germany). *Z. Kinderheilkd.* 114(3):221-232, 1973.

The results of 179 oral d-xylose tests performed in 145 children (3 months-13 1/2 yr old) were compared with the dissecting microscope findings of the jejunal biopsy specimens. All but one of 68 subtotal villous atrophies and 3 of 18 partial villous atrophies were gluten-induced. The majority (57%) of the tests performed on children 3 months to 3 yr old with subtotal villous atrophy were found to yield 1-9% of recovered d-xylose, with a significant difference from the 2 other morphological groups, partial villous atrophy and normal mucosa. All 3 groups overlapped in the range of 10-15% d-xylose test. This means that only a d-xylose test of less than 10% is indicative of celiac disease. Some test values above 15% in children under 3 yr of age with subtotal villous atrophy were the result of a consciously or unconsciously given gluten-free diet prior to biopsy. The regeneration of the mucosa in the upper small intestine proceeds more slowly than the normalization of the d-xylose test. In early childhood the test may be of value in that it may provide evidence of successful gluten-free diet in the first phase of therapy. Villous atrophy in the older child with celiac disease recurring after reintroduction of gluten was never detected with the test. There is no difference between the distribution of d-xylose test in children with normal mucosa and those with partial villous atrophy. The d-xylose recovery in the urine of children with normal mucosa increased with the age of the child.

6707 α_1-FETOPROTEIN IN LIVER DISORDERS AND METABOLIC DISEASES IN CHILDREN. *(Fr.)* Buffe, D.; Rimbaut, C. (Sci. Res. Inst. Cancer, Villejuif, France). *Biomedicine (Paris)* 19:172-176, 1973.

α_1-Fetoprotein (FP) was determined by immunodiffusion and radioimmunodiffusion in sera from 264 children, aged 2 months to 15 yr, with primary or secondary liver tumors and nonmalignant liver diseases. Positive tests for FP were obtained on sera from 39 of 41 children with primary hepatomas. Depending upon its initial level in the serum, FP disappeared within 8 to 20 days after surgical removal of the tumor. The only exceptions were cases in which the tumor had not been completely removed or in which a recurrence developed. Negative tests for FP were obtained in 77 children with hepatic metastases, 6 with hamartomas, 4 with angiomas, 1 with an adenoma, 1 with a hydatid cyst, 2 with traumatic hemobilia, and 62 with hepatomegaly and posthepatitic cirrhosis. Of 40 children with hepatitis, 13 had positive tests for FP. In all but 2 severe cases of hepatitis, FP was found only for a short time and in low concentrations. Of 25 children with metabolic diseases, only 4 of 5 with tyrosinosis had positive tests for FP. In one case, which was followed for 2 1/2 yr, the FP concentration decreased as diet therapy reduced elevated serum methionine and cystine levels; a hepatoma was ruled out at autopsy. A sister of this patient also had the same disorder of amino acid metabolism and a positive test for FP. The one patient with tyrosinosis and a negative test for FP had normal serum methionine levels. FP was not detected in children with frustosemia (5), galactosemia (2), glycogenosis (2), mucopolysaccharidosis (1), glucose-6-phosphate dehydrogenase deficiency (7), pyruvate kinase deficiency (1), Wilson's disease (1), or hemochromatosis (1).

6708 STUDIES ON BILIRUBIN SECRETION IN MAN.

(Ger.) Klapdor, R. (1st Med. Clin., Univ. Hamburg, Germany). *Z. Gastroenterol.* 10(1):27-30, 1972.

Bilirubin secretion was measured on 7 cholecystectomized patients by aspirating the duodenal contents with a triple-lumen balloon catheter every 5-10 min over a period of 90-120 min. Liver function tests and the i.v. cholangiogram were normal in 6 cases; the remaining patient had increased serum bilirubin and alkaline phosphatase values and recurrent choledocholithiasis. Despite interruption of the enterohepatic circulation, the mean bilirubin secretion remained constant at 0.5-2 mg/10 min or 5-10 mg/hr, even in the patient with choledocholithiasis. These results agree with others in the literature. In contrast to investigations performed on patients with gallbladders, the bile secretion remained constant with this method. Determinations can be repeated, which is an advantage over the use of T-tube drains on cholecystectomized patients.

709 DIAGNOSTIC VALUE OF THE AMYLASE DETERMINATION IN ASCITES.

(Ger.) Polak, M.; Torres a Costa, A. C. (Med. Fac., Sao Paulo, Brazil). . *Gastroenterol.* 10(7):561-566, 1972.

sing the method of Myers, Free, and Rosinski, amylase eterminations were made on ascites fluid from 323 atients (177 males and 146 females, aged 1-79 yr) ith a variety of diseases. Amylase activities above 000 Myers U/100 ml were measured in 12 of the 14 atients with chronic pancreatitis. In 3 patients ith primary or secondary pancreatic cancer the mylase activities were 55, 990, and 1000 Myers U/ 00 ml, resp. It is suggested that increased amylase ctivities in pancreatic cancer may be caused by an ssociated process of inflammation. Amylase activi- ies between 10 and 664 Myers U/100 ml were obtained or 306 patients with no evidence of pancreatic isease. These findings confirm that high amylase ctivities in ascitic fluid are diagnostic for ancreatic disease. However, it is pointed out that ome ovarian cysts contain fluid with a very high mylase activity. If such a cyst is mistakenly iagnosed as ascites and drained, amylase activities un on this fluid will give false operative results.

6710 SERUM GAMMA-GLUTAMYL TRANSPEPTIDASE ACTIVITY IN HEPATIC COMPLICATIONS OF CYSTIC FIBROSIS.

(Fr.) Feigelson, J.; Pecau, Y. (no affil.). *Nouv. Presse Med.* 1(28):1899-1900, 1972.

Measurements of serum γ-glutamyl transpeptidase activity, performed over a 6-month period on 32 patients, aged 10 months to 19 yr, with cystic fibrosis showed that elevations in the activity of of this enzyme occurred in 5 patients with symptoms of biliary cirrhosis (mean of 163 international milliunits/ml). Inconsistent or nomal results were obtained in these patients with other serum enzymes commonly used to diagnose liver damage (cholinesterase, SGPT, alkaline phosphatase). The highest value for γ-glutamyl transpeptidase (970 milliunits/ml) was obtained in a 3-yr-old boy with viral hepatitis, the diagnosis of which was confirmed by neutropenia and high SGPT values. This high value, which normalized after 3 months, was probably caused by the additive effects of cholestasis and jaundice. In 2 cases, results of the clinical examination did not agree with those of hepatic scintigraphy; in these cases γ-glutamyl transpeptidase activities were slightly elevated and in the upper normal range resp., but soon decreased. In the remaining 24 patients, most of whom had marked pulmonary signs, serum γ-glutamyl transpeptidase activities were in the lower normal range (mean of 11 milliunits/ml) in 22 or upper normal range (mean of 48 milliunits/ml) in 2. It is concluded that γ-glutamyl transpeptidase is a sensitive and specific test for cholestasis and appears to be a good method for detecting hepatic complications in cystic fibrosis.

6711 PANCREATIC VISUALIZATION WITH THE GAMMA CAMERA BY PHOTOGRAPHIC SUBTRACTION.

(E.) Steven, L. W.; Andrews, J. T.; Chmiel, R. L. (Roy. Melbourne Hosp., Australia). *Aust. Radiol.* 17(1): 40-42, 1973.

The value of pancreatic visualization with the gamma camera has been significantly enhanced with little extra time and expense involved. The patient receives an injection of 250 μC of ^{75}Se-selenomethionine and 2 mC of ^{99m}Tc-sulfur colloid 20 min before the start of the imaging. An exposure time of about 30 min is required to obtain acceptable statistical quality in the ^{75}Se image. The pulse height analyser is tuned to the 270 keV peak in the ^{75}Se spectrum. At the end of this exposure period, the analyser is tuned for the 140 keV peak of ^{99m}Tc and a 2-5 min exposure is made. A photographic reversal is made of the view obtained with the ^{75}Se-selenomethionine and this is superimposed on the ^{99m}Tc colloid liver image (photographic subtraction). Light is then transmitted through both films onto a third unexposed film with the resulting exposure showing the pancreatic outline unobstructed by liver interference. Since this subtraction process is nondestructive, the investigator retains the original images and can better interpret them in light of the subtracted image.

6712 FATAL ENDOTOXIC SHOCK OF BILIARY TRACT ORIGIN COMPLICATING TRANSHEPATIC CHOLANGIOGRAPHY.

(E.) Keighley, M. R. B.; Wilson, G.; Kelly, J. P. (Leeds (St. James's) Univ. Hosp., England). *Br. Med. J.* 3(5872):147-148, 1973.

A 70 yr old male presented with a 5-month history of painless jaundice and elevated serum bilirubin, alkaline phosphatase, SGPT, and prothrombin time. Liver biopsy showed changes of extrahepatic obstruction. A transhepatic cholangiogram showed the extrahepatic biliary tract to be dilated proximal to a stone which was partly occluding the distal end of the common bile duct. Within 1 1/2 hr after cholangiography the patient developed a rigor and became hypotensive with a warm vasodilated peripheral circulation; a transient purpuric rash developed later, but there was no evidence of biliary peritonitis or intra-abdominal bleeding. Despite removal of the stone and administration of antibiotics, hydrocortisone, diuretics, and sodium bicarbonate to correct severe metabolic acidosis, the patient became anuric and went into hepatic coma 3 days after surgery and died. *Escherichia coli* was isolated from blood cultures taken after cholangiography and before surgery, confirming a diagnosis of gram-negative endotoxic shock. *E. coli* was also isolated from the common bile duct at surgery and during cholangiography; the same organism was found in duodenal samples and a liver biopsy taken during surgery. All postoperative blood cultures were sterile. It is concluded that *E. coli* found after cholangiography was of biliary tract origin and was responsible for endotoxic shock. Routine use of bile cultures and antibiotic therapy is recommended for all patients undergoing transhepatic cholangiography to prevent development of this complication.

6713 ENDOSCOPY OF THE ILEOCECAL AREA. *(E.)*

Nagasako, K.; Takemoto, T. (Tokyo Women's Med. Coll., Japan). *Gastroenterology* 65(3):403-411, 1973.

Advances in the field of fiberoptics have resulted in the development of long colonoscopes. This instrument allows observation of the ileocecal area. In 125 cases, a fibercolonoscope was inserted into the ileocecal area under visual control. The last 100 cases were used for this study. The ileocecal sphincter was observed in 81% of these 100 cases, and the terminal ileum in 66%. The normal endoscopic features of the ileocecal sphincter, the root of the appendix, observed in 21% of the cases, the cecum, and the terminal ileum were noted. It appears that in the living subjects the ileocecal sphincter and the root of the appendix are not constant in form but manifest various forms according to intestinal motility. The terminal ileum can be classified into 4 grades (0 to III) according to the mucosal appearance resulting from lymph follicular hyperplasia. In the present series, the extent of lymph follicular hyperplasia varied greatly in inverse proportion to age. Lymph follicular hypoplasia, a common finding in young people, is merely a physiological phenomenon.

6714 RECTOSCOPIC FINDINGS IN ULCERATIVE COLITIS: A SUMMARY OF THE MORPHOLOGY, CYTOLOGY, AND HISTOLOGY.

(Ger.) Dollinger, H. (Ctr. Internal Med. Pediatrics, Univ. Ulm, Germany). *Med. Welt* 23(4):117-120, 1972.

The results of clinical, rectoscopic, histological, and cytological examinations were compared for 16 patients (10 males and 6 females, aged 14-67 yr) with clinical and radiological evidence of ulcerative colitis. On the basis of clinical and rectoscopic findings, patients were classified as having active (5), semiactive (8), or inactive (3) forms of ulcerative colitis. In the active form rectoscopic findings included diffuse mucosal inflammation, punctate to profuse bleeding, ulcers, thickening and flattening of the mucosal folds, and pseudopolyposis. Cytological examination revealed polymorphonuclear leukocytes, plasma cells, and large numbers of eosinophils. Histological findings included mucous exudate in the crypts of Lieberkuhn; accumulations of RBC, neutrophils, and eosinophils; round cell infiltration of the mucosa and submucosa; epithelial erosion and necrosis; mucosal bleeding; and lymphoid hyperplasia in the submucosa. In the semiactive form rectoscopic examination revealed mucosal discoloration, regression or disappearance of mucosal folds, and thickening of the mucosa due to edema and fibrosis. Both inflammatory and epithelial cells were present in cytological preparations, while biopsies revealed erosions, mucosal ulceration, signs of epithelial regeneration, and thickening of the tunica muscularis and muscularis mucosae. Rectoscopic abnormalities in the inactive form were less pronounced and may include mucosal thickening and flattening, fibrosis, and superficial mucosal granulation. Since the mucosa is dry, it is impossible to obtain good smears for cytological examination. Biopsies showed an increase in the number of mucous cells and a decrease in the number of crypts of Lieberkuhn. Edema of the lamina propia, round cell infiltration, submucosal fibrosis, and mucosal granulation were present. Disagreement between clinical and morphological, cytological, or histological findings was found in 1 of 5 patients with acute, 4 of 8 with semiacute, and 3 of 3 with inactive ulcerative colitis. Histological examinations appear to be most indicated in patients with the inactive form of ulcerative colitis since cytological examinations give negative results in these patients.

6715 THE ACID-BARIUM TEST AS AN INDEX OF INTERMITTENT GASTRO-OESOPHAGEAL REFLUX.

(E.) McCall, I. W.; Davies, E. R.; Delahunty, J. E. (United Bristol Hosp., England). *Br. J. Radiol.* 46(548):578-584, 1973.

The acid-barium test for esophageal peristalsis was performed on 350 patients and the results compared with the clinical evidence of reflux. The test correlated only moderately well with the clinical features, mainly because of unexpected positive tests in patients without other evidence of reflux.

It is concluded that although the test detects sensitivity of the esophagus to acid perfusion, a positive test does not necessarily indicate symptomatic reflux. However, the test may be of value as a screening procedure for confirming the nature of symptoms thought to be due to reflux; for assessing the significance of hiatus hernia without overt reflux; for assessing symptoms associated with gastroesophageal reflux after excluding more common causes; and for selecting patients for more complicated tests of esophageal function.

6716 THE VALUE OF PERCUTANEOUS CHOLANGIOGRAPHY. *(E.)* Evison, G.; McNulty, M.; Thomson, C. (Roy. United Hosp., Bath, England). *Postgrad. Med. J.* 49(575):637-640, 1973.

Percutaneous cholangiograms were obtained on 50 patients with surgical or autopsy diagnoses of carcinoma of the pancreas (24), gallstones (6), hepatitis (2), chlorpromazine jaundice (1), liver metastases (2), carcinoma of the gallbladder (2), carcioma of the common bile duct (3), inflammatory mass n the pancreas (2), stone(s) in the common ile duct (2), infectious hepatitis (1), strictures n the common bile duct (4), and pancreatic abscess 1). Of these 50 patients, 45 were clinically hought to have extrahepatic obstruction; this was onfirmed in 33 cases by cholangiogram. Of the ther 12 cases with no cholangiographic evidence f obstruction, 9 did not have extrahepatic obstrucion at surgery or autopsy, while the remaining 3 did. n these 3 cases the intrahepatic ducts were not ilated although the common bile duct was distended. ailure to puncture a duct almost certainly means hat the ducts are not dilated, but this does not ecessarily mean that there is no extrahepatic ostruction. In the 5 cases clinically thought to e nonobstructive, cholangiograms showed all were ostructed. The additional information provided by he percutaneous cholangiogram materially increases he accuracy of the preoperative diagnosis. The olangiogram should be done preoperatively since he quality of the radiography obtained at operation s not as good.

717 INTRAPERITONEAL LIPASE AND TRYPSIN. IMPORTANCE OF THEIR DETERMINATION IN DRAINAGE LUIDS AFTER ABDOMINAL SURGERY. *(Fr.)* Perissat, J.; marelle, C.; Doutre, L. P. (St. Andre Hosp., rdeaux, France). *Arch. Fr. Mal. App. Dig.* 62(4): 3-307, 1973.

easurements of lipase and trypsin activity were made n peritoneal fluid, obtained during drainage, from patients who had undergone abdominal surgery. ese included 19 patients who had undergone surgery ich did not involve the pancreas (group I), 20 in om the pancreas was mobilized but the capsule was t broken (group II), 23 with diseases involving the ncreatic parenchyma (group III), 11 with acute crotizing pancreatitis (group IV), and 10 with pancreatic fistulas (group V). Lipase activities were not appreciably increased (above 10 Vogel-Zieve U) in any patients belonging to groups I-III, but lipase activities were increased in 31 of 36 determinations made on patients in group IV and in 25 of 26 made on patients in group V. The difference in lipase activities between group IV and V and groups I-III was highly significant. Increased trypsin activities (above 20 IU) were found in 13 of 34 determinations made on patients in group IV and in 18 of 27 made on patients in group V; trypsin activities were not significantly increased in groups I-III. A significant difference was found between trypsin activities in groups I-III and those in groups IV and V, but the difference was not as great as that for lipase activities. High lipase and trypsin activities in peritoneal fluid from patients who have undergone surgery which does not involve the pancreas is suggestive of, but not diagnostic for, acute postoperative hemorrhagic necrotizing pancreatitis or a pancreatic fistula.

6718 DIAGNOSIS OF JAUNDICE CAUSED BY EXTRAHEPATIC OBSTRUCTION OF THE BILIARY TRACT: STUDY OF LIPIDS AND LIPOPROTEINS IN AU SERUM. *(Fr.)* Fruchart, J. C.; Sezille, G.; Jaillard, J.; Paris, J. C.; Biserte, G. (Med. Clin. West, Munic. Hosp., Lille, France). *Nouv. Presse Med.* 2(22):1505-1508, 1973.

The value of serum lipid and lipoproteins as diagnostic methods for obstructive jaundice was investigated in 40 patients with extrahepatic biliary obstruction (18 with tumors compressing the biliary tract and 22 with cholelithiasis); 63 patients with viral hepatitis served as controls. Mean serum free cholesterol and phospholipids were highest in patients with tumors and lowest in those with viral hepatitis. Phospholipid concentrations of 18-20 g/liter were found in 11 patients with tumors, but elevated phospholipids are not specific for this form of obstructive jaundice. Migration of α-lipoproteins on electrophoresis was very slow (28%) or did not occur (72%) in patients with complete biliary obstruction, but this phenomenon was also observed in 3% and 20%, resp. of patients with hepatitis. The Jirgl flocculation test was not specific for obstructive jaundice; it was positive in 83% of the patients with obstructive jaundice and in 21% of those with hepatitis. Semiquantitative determinations of lipoprotein X were made by determining the ratio of antigenically specific β-lipoproteins by radial immunodiffusion to lipoproteins found in normal serum by heparin flocculation in the presence of calcium chloride. This ratio was more than 2 in 45% of patients with tumors, in 14% of those with cholelithiasis, and in none of those with viral hepatitis. Values above 3 were found only in patients with tumors, particularly in those with carcinomas of the head of the pancreas. Thus, lipoprotein X is the most specific method for diagnosing obstructive jaundice.

6719 EXPERIENCE WITH THE ENTAMOEBA HISTOLYTICA FLUORESCENT ANTIBODY TEST IN WESTERN AUSTRALIA. *(E.)* Norcott, T. C. (Roy. Perth Hosp., Australia). *Med. J. Aust.* 2(1):21-22, 1973.

Immunofluorescence serology was used in the diagnosis of cases of extra-intestinal *Entamoeba histolytica* infections. Sera from 138 patients were tested. Of these 138, 17 had titers of 1:32 higher Clinical diagnoses in these cases included hepatic amebiasis (10), intestinal and hepatic amebiasis (1), secondary pyogenic infection of an amebic liver abscess (1), ameboma (1), amebic dysentery (1), hemangiomas of the liver and left kidney (1), enlarged liver with intestinal parasites (1), and amebic colitis (1). Most of these 17 patients had resided or traveled in Asia. In this series when the titers exceeded 1:128, the infection was extra-intestinal. Since serodiagnosis is reliable, aspiration of an amebic liver abscess solely for diagnostic purposes is not justified. Because of the slow decline in antibody levels, this test cannot be used as a reliable short-term guide to the success of treatment.

6720 A DIRECT APPROACH TO THE DIFFERENTIAL DIAGNOSIS OF JAUNDICE. LAPAROSCOPY WITH TRANSHEPATIC CHOLECYSTOCHOLANGIOGRAPHY. *(E.)* Berci, G.; Morgenstern, L.; Shore, J. M.; Shapiro, S. (Cedars of Lebanon Hosp., Los Angeles, Calif.). *Am. J. Surg.* 126(3):372-378, 1973.

A percutaneous transhepatic cholecystocholangiogram has been devised using double guidance by laparoscopy and x-ray image amplification as an aid in differential diagnosis of jaundice. This procedure was employed in 3 cases of painless progressive jaundice. In a 54-yr-old male serum bilirubin rose from 8-13 mg%; alkaline phosphatase was 53 King-Armstrong U. Malignant biliary obstruction was suspected, but laparoscopy and percutaneous transhepatic cholecystocholangiography displayed a normal gallbladder and nonobstructed extrahepatic biliary tree. Liver biopsy showed cholestasis. In a 48-yr-old male serum bilirubin rose from 15 to 18 mg% during observation; alkaline phosphatase was 60 King-Armstrong U. Laparoscopy and percutaneous transhepatic cholecystocholangiography revealed extrinsic obstruction of the distal common bile duct. Laparotomy confirmed pancreatic carcinoma. In a 37-yr-old male serum bilirubin rose from 7 to 33 mg%; alkaline phosphatase was 46 King-Armstrong U; SGOT, 524; and SGPT, 184. Evidence for both biliary lithiasis and parenchymal liver disease existed. Laparoscopy and percutaneous transhepatic cholecystocholangiography revealed the patient had 2 distinct clinical entities, phenothiazide-induced jaundice and nonobstructive cholelithiasis. The advantages of laparoscopic transhepatic cholecystocholangiography over other available methods of direct cholangiography are direct visual diagnosis; biopsy under visual control; radiographic demonstration of biliary tract in the absence of duct dilatation; immediate laparotomy when indicated; and control of bile leak and/or bleeding under direct vision.

6721 REMNANT CYSTIC DUCT IN T-TUBE CHOLANGIOGRAPHY. *(E.)* Lewicki, A. M.; Kleinhaus, U.; Ozer, H. (Harvard Med. Sch., Boston, Mass.). *Am. J. Roentgenol. Radium Ther. Nucl. Med.* 119(1): 52-56, 1973.

An analysis was made of 70 postoperative T-tube cholangiograms. Cystic duct remnants were found in 44 cases (63%) and were just as likely to be left incompletely excised whether they were angular or parallel in type. Those left in the parallel group were, however, significantly longer. The overall incidence of remnants as well as the mean lengths of those which cannot be excised completely will undoubtedly be reduced by the application of cholangiographic techniques in the operating room similar to those presently available in the postoperative setting. A medially running remnant is much more intimately associated with a common hepatic duct than other types. Although such a remnant is frequently difficult and sometimes impossible to resect, it probably also causes extrahepatic obstruction early with only minimal dilatation.

6722 FURTHER OBSERVATIONS ON α-FETOPROTEIN IN THE DIAGNOSIS OF DISEASES OF THE DIGESTIVE TRACT. *(E.)* Nishioka, M.; Okamoto, Y.; Shigeta, K.; Hironaga, K.; Fujita, T. (Yamaguchi Univ. Sch. Med., Ube, Japan). *Digestion* 8(5):396-406, 1973.

α-Fetoprotein was measured in the sera from 183 patients with malignancies, including primary hepatocellular carcinoma (37); cholangiocellular carcinoma (2); carcinoma of liver metastasized from stomach (76); carcinoma of the esophagus (2), stomach (22), colon (6), rectum (4), lung (6), gallbladder (1), pancreas (6), kidney (2), ovary (4), testis (3); reticulosarcoma (3); Hodgkin's disease (3), and leukemia (6); 368 patients with nonneoplastic liver diseases served as controls. α-Fetoprotein was detected in 33 of the patients with primary hepatocellular carcinoma, in 4 of those with carcinoma of the liver metastasized from the stomach, in 1 with gastric carcinoma, and in 1 with ovarian carcinoma. α-Fetoprotein was also detected transiently in 1 patient with infectious hepatitis and in 5 with cirrhosis. The frequency of α-fetoprotein-positive patients increased when more sensitive techniques were used, such as immunoelectrosyneresis and fluoroelectroimmunodiffusion. However, it is important to use the monospecific antiserum prepared by immunization against purified α-fetoprotein. The maximal concentration of α-fetoprotein in sera from patients with primary liver carcinoma was 5,900 μg/ml serum. The α-fetoprotein levels in the majority of these patients were in the range of 10-500 μg/ml. Serum α-fetoprotein levels increased with time, but were unrelated to clinical signs or survival time. In patients with carcinoma of the liver metastasized from the stomach, gastric carcinoma, and nonneoplastic liver diseases, serum α-fetoprotein levels were significantly lower than those in primary hepatocellular carcinoma.

6723 A COMPARATIVE STUDY OF FOUR TESTS OF PANCREATIC FUNCTION IN THE DIAGNOSIS OF PANCREATIC DISEASE.

(E.) Youngs, G. R.; Agnew, J. E.; Levin, G. E.; Bouchier, I. A. D. (Roy. Free Hosp., London, England). *Q. J. Med. (New Series)* 42(167):597-618, 1973.

The conventional and subtraction pancreas scans, the Lundh test, and the radioselenium test of pancreatic function were performed in 80 patients to clarify the indications for performing 1 or more of these tests in the diagnosis of pancreatic disease. Diagnosis included carcinoma of the head of the pancreas (14), sarcoma of the head of the pancreas (1), carcinoma of the body of the pancreas (5), obstructive jaundice due to supra-ampullary bile duct obstruction (5), obstructive jaundice due to peri-ampullary bile duct obstruction (3), diabetes mellitus (5), secondary carcinoma of the liver (4), hemochromatosis (4), peptic ulcer (3), intestinal malabsorption (2), and alcoholic cirrhosis (1). No biochemical or radiological evidence of pancreatic disease was detected in 19 subjects. All four tests were performed simultaneously in a single two-hour session. The scans were marked blindly by three independent observers. The radioselenium and Lundh tests were equally accurate in distinguishing between normal and abnormal pancreas. Thus only 1 of these tests need be performed. Routine performance of both a conventional and a subtraction scan is, however, indicated because the subtraction scan gave fewer false positive results in normal patients, whereas the conventional scan yielded better resolution of filling defects. A normal pancreatic scan indicated a 94% probability that the pancreas was normal. If the scan was normal the intubation test was always normal. An abnormal intubation test indicated a 100% probability that the pancreas was abnormal. If the intubation test was abnormal the scan was always abnormal. However, abnormal (false-positive) scans were seen in 25% of the normal subjects and normal (false-negative) intubation tests were seen in 35% of patients with pancreatic carcinoma. Abnormal scans occurred in 95% of patients with pancreatic carcinoma and in some instances the scans were very suggestive of carcinoma since a localized filling defect was seen. Thus the pancreatic scan is more reliable than an intubation test in establishing a diagnosis of pancreatic carcinoma. Diagnostic results can be improved by performing either one of the duodenal intubation tests together with both the conventional and the subtraction scan. However, for some patients, either the scans on their own (if normal) or an intubation test alone (if abnormal) will suffice.

6724 A NEW APPROACH IN THE PERFORMANCE OF GASTRIC ANALYSIS.

(E.) Diaz, F. J.; Meeroff, M. (Dept. Gastroenterol., Sanatorio Metropol., Buenos Aires, Argentina). *Am. J. Gastroenterol.* 60(3):265-272, 1973.

Gastroionogram, a procedure for gastric analysis based on the measurement of acidity and principal ion concentrations in gastric juice, was used in the study of 40, aged 18-55 yr, normal male subjects. After a 12 hr fast and aspiration of residual gastric contents, basal secretion was collected during 1 hr. An antihistamine agent was injected i.m. 15 min before the end of this hr. One hr after aspiration was begun, histamine dihydrochloride (0.024 mg/kg) was injected. The initial 15 min collection was discarded. Subsequent sample volumes were measured and concentrations of electrolytes determined. As expected under neutral conditions, an exact relation was established among the principal ions of the gastric juice in 60% of the cases; in the other 40%, the variation was exceedingly slight. After stimulation, all parameters, except sodium output, changed significantly. Net increases occurred in volume, hydrogen ion concentration, total acidity, acidity output, potassium output, chloride concentration, and chloride output. Potassium concentration showed a very small increase. Undissociated acid and sodium decreased after stimulation. It is suggested that the relations among these various parameters change during pathological situations and may be thus helpful in the management of gastrointestinal diseases.

6725 COMPARISON OF THE ACCURACY OF LIVER SCANS AND PERITONEOSCOPY IN BENIGN AND MALIGNANT PRIMARY AND METASTATIC TUMOURS OF THE LIVER. 222 CONFIRMED CASES EXAMINED BY BOTH METHODS SIMULTANEOUSLY.

(E.) Sauer, R.; Fahrlander, H.; Fridrich, R. (Dept. Nucl. Med., Univ. Basel, Switzerland). *Scand. J. Gastroenterol.* 8(5):389-394, 1973.

The accuracy of liver scanning and peritoneoscopy was compared in 123 patients with primary or metastatic tumors, including a few benign localized lesions. The lesions consisted of adenocarcinoma (47), squamous cell carcinoma (10), oat cell carcinoma (7), linitis plastica of stomach (1), adenocarcinoma of the kidney (2), melanoma (2), Hodgkin's disease (2), reticulum cell sarcoma (1), hepatoma (25), liver cysts (6), hepatic echinococcus (3), liver abscess (3), liver hemangioma (1), and periarteritis nodosa (1); 99 patients had no such lesions. All findings were histologically verified by biopsy, operation, or necropsy. Using each method alone, the incidence of false-negative findings was 20% for each. False-positive findings were 18% for liver scans and 0% for peritoneoscopy supplemented by target biopsy. By using both methods together, the incidence of false-negative findings was reduced to 7% and false-positive results were eliminated. Thus, the liver scan and peritoneoscopy should be combined to document space-occupying lesions of the liver. Liver scanning can differentiate cirrhosis from neoplastic liver disease.

6726 RETICULO-ENDOTHELIAL AND BLOOD-POOL SCANNING IN THE DIAGNOSIS AND DIFFERENTIATION OF SPACE OCCUPYING LESIONS OF THE LIVER.

(E.) Andrews, J. T.; Steven, L. W.; Arkles, L. B.; Sephton, R. G.; Martin, J. J. (Roy. Melbourne Hosp., Australia). *Aust. N.Z. J. Surg.* 43(1):14-18, 1973.

An attempt was made to differentiate neoplastic from non-neoplastic space-occupying lesions of the liver by a combination of reticuloendothelial and blood-pool scanning. Of a group of 100 patients studied, 45 had clearly visible space-occupying lesions. The vascularity of the lesions was quantitatively assessed in 31 cases. Diagnoses in these 31 included hydatid disease (6); polycystic liver (1); amebic abscess (2); *Staphylococcus aureus* abscess (1); pyrogenic abscess (1); secondary carcinomas of the prostate (1), colon (2), breast (2), nasopharynx (1), pancreas (1), lung (1), eye (1), rectum (1), and thyroid (1); secondary carcinoma with primary unknown (4); secondary carcinoid tumor (1); lymphosarcoma (1); multicentric hepatoma (1); hepatoma (1); and leiomyosarcoma (1). Cysts and abscesses were shown by this technique to be avascular; 14 tumors were demonstrably vascular, though to varying degrees, while 6 were essentially avascular. Therefore, in interpreting the hepatic scan when this combined technique is used, a vascular or partly vascular appearance would weight the diagnosis toward tumor rather than abscess or cyst. Quantitative assessments of vascularity could not be made when the lesion was not completely surrounded by liver tissue or when it lay over another vascular area, e.g. the aorta.

6727 PRELIMINARY EVALUATION OF "DUODENITIS" BY ENDOSCOPY AND BIOPSY.

(E.) Cotton, P. B.; Price, A. B.; Tighe, J. R.; Beales, J. S. M. (St. Thomas's Hosp., London, England). *Br. Med. J.* 3(5877):430-433, 1973.

A study was made of 51 patients (41 male and 10 female; aged 12-76 yr) with dyspeptic symptoms or bleeding in whom endoscopy revealed congested and irregular areas of duodenal bulb mucosa in the absence of ulcer or scar. Biopsy revealed unequivocal active inflammation (epithelial cell atypia and neutrophil infiltration) in 22 of these patients, but in none of 29 control patients with an endoscopically normal bulb. There were no reliable radiological markers of active duodenitis. These patients, and a group of 25 with known duodenal ulcers (21 male and 4 female; aged 19-73 yr), shared similar clinical characteristics and a high incidence of gastric metaplasia in the bulb. In the short follow-up period most patients with active duodenitis remained symptomatic; 2 developed ulcers, and 2 others have undergone vagotomy and pyloroplasty, with poor short-term results. The clinical significance of visual and histological mucosal changes, and their relation to ulcer disease, merit long-term study.

6728 CHOLEDOCHOSCOPY IN CHOLEDOCHOLITHIASIS.

(E.) Longland, C. J. (Roy. Infirm., Glasgow, Scotland). *Br. J. Surg.* 60(8):626-628, 1973.

Endoscopic examinations were performed with a flexible fiber-optic choledochoscope at 37 operations on 35 patients, aged 19-74 yr, to look for residual stones after choledocholithotomy and to explore ducts in which no direct evidence of stones could be obtained by palpation or radiography. Stones were found during 26 operations on 24 patients, and no stones were present in the remaining 11. No false positive results were obtained, but 6 stones remained undetected. After choledocholithotomy residual stones were detected by choledochoscopy in 11 of 24 operations. Except for 3 cases in which stones could not be removed and choledochoduodenostomies were performed to facilitate their escape, residual stones were removed by repeated choledochoscopy. Choledochoscopy provided additional diagnostic information in 8 other cases in which preoperative cholangiography was inconclusive or not available. No complications or sepsis occurred, and no patients died; no special precautions were taken. It is concluded that choledochoscopy should be used in conjunction with operative cholangiography to diagnose retained stones.

6729 COLONOSCOPY IN THE DIFFERENTIAL DIAGNOSIS OF CARCINOMA FROM DIVERTICULITIS OF THE SIGMOID COLON.

(E.) Dean, A. C. B.; Newell, J. P. (Dept. Surg., Univ. Edinburgh, Scotland). *Br. J. Surg.* 66(8):633-635, 1973.

Colonoscopy was successfully performed on 19 of 37 patients (22 females and 15 males, aged 59-84 yr) who had sigmoid diverticula with a narrowed segment suspected of being a carcinoma. Carcinomas were detected in 4 and definitively ruled out in 5 cases; in 9 cases the suspicious segment could not be examined in its entirety, but enough was seen for carcinoma to be ruled out with a reasonable degree of confidence. In follow-ups ranging from 6 months to 2 yr no carcinomas developed in any of the 14 patients with negative findings on colonoscopy. In 1 patient colonoscopy gave a false-negative result; laparoscopy performed 2 weeks later showed that the bowel was invaded by transperitoneal spread from a carcinoma of the stomach. Colonoscopic examination was a failure in 17 cases, usually because the instrument could not be passed into the diseased segment because of a sharp angulation of the bowel; inadequate bowel preparation was also responsible for failure in 3 cases.

6730 PANCREATOGRAPHIC ABNORMALITIES DUE TO PANCREATIC CANCER.

(E.) Norton, R. A.; Ogoshi, K.; Hara, Y.; Niwa, M.; Paul, Jr., R. E.; Tomas, J.; Fawaz, K. (New England Med. Ctr. Hosp., Boston, Mass.). *Gastrointest. Endosc.* 21(1):13-14, 1973.

The endoscopic cannulation records of 2 medical centers were studied for evidence of pancreatic cancer. Of 483 pancreatic ductograms, 33 were characteristic for pancreatic carcinoma and fell into 4 patterns; stenotic (12), tapering (5), obstructed (15), or unclassified (1). The pattern of retrograde pancreatograms in both the stenotic and obstructed types may result from a locally expanding or invading tumor, with the stenotic type as the earlier partially obstructed phase and the latter as the completely obstructed phase. The pattern in the tapering type of pancreatic carcinoma represents a more diffusely infiltrating tumor than the other 2 types. False-positive patterns were caused by 3 conditions: idiopathic chronic pancreatitis, surgical mobilization of the head of the pancreas and traumatic pancreatitis. No false-negative results have been found in a brief followup period. The endoscopic method remains valid for preoperative diagnosis of pancreatic cancer, if these sources of false-positive results are kept in mind.

6731 ENDOSCOPIC RETROGRADE CHOLANGIOGRAPHY. EXPERIENCE OF 168 EXAMINATIONS. *(E.)*

Safrany, L.; Tari, J.; Barna, L.; Torok, I. (Semmelweis Univ. Med. Sch., Budapest, Hungary). *Gastrointest. Endosc.* 19(4):163-168, 1973.

Endoscopic retrograde cholangiography performed in 168 patients (92 females and 76 males, aged 19-82 yr) with suspected biliary disorders was valuable in detecting abnormalities not readily established by excretion methods. Jaundice was present in 117 cases with serum bilirubin levels ranging from 2.0 to 42.0 mg/100 ml. Cholecystectomy had been performed in 81, and 22 had cholangiodigestive anastomoses. This method allowed accurate and detailed radiographic demonstration of the biliary system even in the most intricate cases. Diagnoses obtained by endoscopic retrograde pancreatograms and cholangiograms included: normal biliary system (29), primary biliary cirrhosis (15), hypertrophy of the sphincter of Oddi (9), benign (cicatricial) narrowing of the common bile duct (16), gallbladder stones (4), common bile duct stones (50), cancer of the head of the pancreas (11), pancreatic fibrosis (2), primary cancer of the biliary system (8), cholangiodigestive anastomosis with normal bile tract (7), cholangiodigestive anastomosis with intrahepatic stone formation (3), cholangiodigestive anastomosis and liver abscess (2), and cancer of the papilla of Vater (2). A significant advantage of the endoscopic retrograde cholangiography is its practicability in patients with impaired excretory function of the liver, such as in advanced jaundice. It is suggested that this technique be performed in patients presenting with biliary disorders, the exact nature of which cannot be revealed by conventional methods.

6732 DETECTION OF HEPATITIS-B ANTIGEN BY RADIOIMMUNOASSAY IN CHRONIC LIVER DISEASE AND HEPATOCELLULAR CARCINOMA IN GREAT BRITAIN. *(E.)*

Reed, W. D.; Eddleston, A. L. W. F.; Stern, R. B.; Williams, R.; Zuckerman, A. J.; Bowes, A.; Earl, P. M. (King's Coll. Hosp., London, England). *Lancet* (7831):690-693, 1973.

Of 264 patients with active chronic hepatitis (94 patients), primary biliary cirrhosis (45), cryptogenic cirrhosis (39), alcoholic cirrhosis (67), and hepatocellular carcinoma (38), a sensitive radioimmunoassay technique showed 37 cases were positive for hepatitis B antigen (HBAg). Of these 37 patients, 20 were HBAg negative by immunodiffusion and electrophoresis. Of the 94 active chronic hepatitis cases, 18% were HBAg positive. Comparison of these cases with HBAg-negative cases showed a higher frequency of HBAg in males and those born overseas. There were no significant differences between HBAg-positive and -negative patients for clinical manifestations, immunoglobulins, autoantibodies (after allowing for differences in sex ratio), cell-mediated immunity, or prognosis, and in some cases the progression of tissue damage in this condition may be unrelated to the continued presence of circulating HBAg. HBAg was found in only 1 patient with primary biliary cirrhosis, and coincidental infection following blood-transfusion was a possibility in half of the HBAg-positive cases of cryptogenic cirrhosis. However, blood-transfusions could be implicated in only 2 of the 6 HBAg-positive patients with alcoholic cirrhosis. In primary hepatocellular carcinoma, 23% of the patients were positive, the frequency being higher (66%, compared with 15%), in those born overseas. Thus, the reported geographical variation in this association cannot be due entirely to differences in the technique employed for detecting HBAg.

6733 DELAYED DUCTAL DRAINAGE: AN ENDOSCOPIC PANCREATOGRAPHIC SIGN OF CARCINOMA OF THE HEAD OF THE PANCREAS.

(E.) Belsito, A. A.; Cramer, G. G.; Dickinson, P. B. (Bethesda Lutheran Med. Ctr., St. Paul, Minn.). *Am. J. Roentgenol. Radium Ther. Nucl. Med.* 119(1):109-114, 1973.

Carcinoma of the pancreas was studied by duodenoscopy and varying degrees of retrograde pancreatography in 16 patients. The roentgenographic technique consisted of immediate filming after injection and 20 min follow-up studies to assess contrast medium retention. Failure of the pancreatic duct to drain on a 20 min delayed film was taken to be indicative of carcinoma of the head of the pancreas. Benign noncalculous chronic pancreatitis, which can have a pancreatographic appearance anatomically similar to carcinoma, was distinguished by its nonobstructed draining characteristics. All of the patients with delayed ductal drainage had confirmed adenocarcinoma of the head of the pancreas; 2 of these lesions were small, resectable carcinomas.

6734 AUTOMATED CONTINUOUS-FLOW HEMAGGLUTINATION INHIBITION TEST FOR HEPATITIS B ANTIGEN IN BLOOD.

(E.) Kwak, K. S.; Sturgeon, P.; Gitnick, G. L. (Gwynne Hazen Cherry Mem. Labs., Los Angeles, Calif.). *Vox Sang.* 25(2):97-104, 1973.

6735 GASTRIC EXFOLIATIVE CYTOLOGY. A RAPID METHOD - PRELIMINARY REPORT.

(E.) Katz, S.; Boyle, C. C.; Sherlock, P.; Winawer, S. J.

(Cornell Med. Sch., Ithaca, N.Y.). *Am. J. Gastroenterol.* 60(2):157-159, 1973.

6736 CANNULATION OF THE AMPULLA OF VATER. *(E.)* Gregg, J. A. (Harvard Univ. Med. Sch., Boston, Mass.). *Am. J. Gastroenterol.* 60(2):142-156, 1973.

6737 STUDIES OF ACID PRODUCTION IN PEPTIC ULCER. *(E.)* Weidner, Jr., M. G.; Yarborough, III., D. R.; Miller, C. P.; Barnes, M. (Med. Univ. South Carolina, Charleston). *South. Med. J.* 66(9):975-980, 1973.

6738 A NEW TUBE FOR USE IN THE FLUORESCEIN STRING TEST: LOCALIZATION OF OESOPHAGEAL AND GASTRIC BLEEDING SITES WITH OR WITHOUT THE USE OF RADIOGRAPHY. *(E.)* Pittman, E. (Med. Univ. South Carolina, Charleston). *Gut* 14(8):669-670, 1973.

6739 IMMUNOFLUORESCENCE IN EARLY DETECTION OF SALMONELLA TYPHI. *(E.)* Mahajan, R. C.; Chitkara, N. L.; Ganguly, N. K.; Sharma, S. (Inst. Med. Ed. Res., Chandigarh, India). *Bull. Postgrad. Inst. Med. Ed. Res. Chandigarh* 6(4):151-154, 1972.

6740 THE PLACE OF RADIOLOGICAL INVESTIGATION IN THE DIAGNOSIS OF HYDATID CYST OF THE LIVER. *(It.)* Dayras, M.; Dubrisay, J. (Hosp. Laennec, Paris, France). *Sem. Hop. Paris* 49(23):1657-1666, 1973.

6741 EMERGENCY PERITONEOSCOPY. (REPORT OF 1,265 CASES). *(Fr.)* Llanio, R.; Sotto, A.; Jimenez, G.; Quintero, M.; Ferret, O.; Manso, E.; Nodarse, O. (Inst. Gastroenterol., Havana, Cuba). *Sem. Hop. Paris* 49(12):873-877, 1973.

6742 UPPER GASTROINTESTINAL BLEEDING IN PATIENTS WITH ALCOHOLIC CIRRHOSIS. *(Fr.)* Miniconi, P.; Oudae, P.; Perrin, D.; Delumeau, C.; Leschallier de Lisle, L. R.; Dedieu, P.; Provost, P. (Saint-Jacques Hosp., Nantes, France). *Arch. Fr. Mal. App. Dig.* 62(2):133-139, 1973.

6743 SCINTIGRAPHIC STUDIES OF HEPATIC ABSCESSES. TWENTY CASES. *(Fr.)* Batisse, R.; Ducloux, J. M.; Debonniere, C.; Bocquet, M.; Bosch, A.; Garreta, L. (Serv. Electroradiol. Val-de-Grace, Paris, France). *Ann. Radiol. (Paris)* 16(5-6):331-340, 1972.

6744 FIBRE ENDOSCOPY OF THE OPERATED STOMACH. REPORT OF 253 PATIENTS. *(Fr.)* Coffin, J. C.; Liguory, C.; Capelle, P. (Hosp. St. Antoine, Paris, France). *Sem. Hop. Paris* 49(8):549-533, 1973.

6745 MODERN DIAGNOSIS OF LIVER FUNCTION IN THE CHEMICAL LABORATORY. PART I. DISTURBANCES OF LIVER CELL INTEGRITY AND METABOLIC EFFICIENCY. *(Ger.)* Kuntz, E. (Lutheran Deaconess Hosp., Schwabisch Hall, Germany). *Munch. Med. Wochenschr.* 114(16):781-788, 1972.

6746 SCINTIGRAPHIC DIAGNOSIS OF HEPATIC INVOLVEMENT IN MALIGNANT LYMPHOMAS. *(Ger.)* Erbe, W.; Freisenhausen, H. D. (Radiol. Clin., Univ. Hamburg, Germany). *Strahlentherapie* 144(4):414-420, 1972.

6747 DIAGNOSTIC SIGNIFICANCE OF TUBELESS EXAMINATION OF GASTRIC JUICE ACIDITY BY MEANS OF THE ACIDOTEST. *(Rus.)* Nogaller, A. M.; Ladneva, G. A. (Ryazan Med. Inst., USSR). *Vrach. Delo* 4:10-14, 1973.

6748 STUDY OF ACID FORMATION FUNCTION OF THE STOMACH BY MEANS OF INTRAGASTRIC pH-METRY. *(Rus.)* Pantsyrev, Y. M.; Ageichev, V. A.; Kliminsky, I. V.; Makeeva, N. S.; Novoselets, S. A.; Matafonova, L. F. (N. I. Pirogov 2nd Moscow Med. Inst., USSR). *Klin. Med. (Mosk.)* 50(7):43-46, 1972.

6749 MODERN DIAGNOSIS OF LIVER FUNCTION IN THE CHEMICAL LABORATORY. PART II. DISTURBANCES OF THE EXCRETORY FUNCTION OF THE LIVER AND OF THE MESENCHYME AND RES REACTIONS. *(Ger.)* Kuntz, E. (Lutheran Deaconess Hosp., Schwabisch Hall, Germany). *Munch. Med. Wochenschr.* 114(17):830-835, 1972.

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6755 RETROGRADE PANCREATOCHOLANGIOGRAPHY BY CANNULATION OF THE AMPULLA OF VATER WITH A FIBEROPTIC DUODENOSCOPE. *(Rus.)* Vasil'ev, Iu. V.; Savrasov, V. M.; Sal'man, M. M.; Malkerova, N. N.; Sokolova, G. N. (All-Union Sci. Res. Inst. Gastroenterol., Moscow, USSR). *Klin. Med. (Mosk.)* 50(7): 36-39, 1972.

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6759 ULTRASONIC LIVER SCANNING: AUTOMATED A-SCAN ANALYSIS. *(E.)* Mountford, R. A.; Halliwell, M.; Atkinson, P. (Dept. Med., Univ. Bristol, England). *Phys. Med. Biol.* 18(4):559-569, 1973.

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6761 INTESTINAL ABSORPTION OF RADIOACTIVE VITAMIN B_{12}: A COMPARISON OF PLASMA, FAECAL AND URINARY TESTS. *(E.)* Mathan, V. I.; Swarnabai, S.; Baker, S. J. (Christian Med. Coll. Hosp., Vellore, India). *Indian J. Med. Res.* 61(5):714-723, 1973.

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6773 BACTEREMIA AFTER LIVER BIOPSY. *(E.)* McCloskey, R. V.; Gold, M.; Weser, E. (Albert Einstein Med. Ctr., Philadelphia, Pa.). *Arch. Intern. Med.* 132(2):213-215, 1973.

6774 THE EXTRAHEPATIC UPTAKE OF RADIOACTIVE COLLOIDAL GOLD IN CIRRHOTIC PATIENTS AS AN INDEX OF LIVER FUNCTION AND PORTAL HYPERTENSION. *(E.)* Millette, B.; Chartrand, R.; Lavoie, P.; Viallet, A. (Hosp. St. Luc, Montreal, Canada). *Am. J. Dig. Dis.* 18(8):719-728, 1973.

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6780 STUDIES ON GASTRITIS IN THE UPPER PORTION OF STOMACH BY ENDOSCOPIC CONGO RED TEST. *(E.)* Tatsuta, M.; Saegusa, T.; Okuda, S. (Ctr. Adult Dis., Osaka, Japan). *Endoscopy* 5(2):61-69, 1973.

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See also, 6922, 7011, 7056, 7252, 7349, 7370, 7398, 7402, 7430, 7502, 7612, 7863, 7970, 8060, 8064.

GASTROINTESTINAL DISEASES

ESOPHAGUS

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SYMPTOMATIC PEPTIC OESOPHAGITIS. *(E.)*
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double-blind crossover trial of metoclopramide
0 mg 3 times a day) in 15 patients (10 women and
men, aged 41-72 yr) with severe symptomatic re-
ux esophagitis is reported. Most patients were
derly with a long history of heartburn and regur-
tation. Patients with peptic ulcer were excluded.
significant improvement in symptoms was recorded
ile the patients were on the 'active' agent. Im-
ovement occurred in 8 patients while on the trial,
d 6 of these picked the 'active' month as their
st. The results of this trial suggest that its
ilure could be due to the short action of the
ug, poor timing or dosage, or the severity of
mage to the esophageal sphincter in these patients.

95 PHARMACOLOGICAL PREVENTION OF ESOPHAGEAL
STRICTURE: AN EXPERIMENTAL STUDY IN THE
T. *(E.)* Saedi, S.; Nyhus, L. M.; Gabrys, B. F.;
sakari, K.; Bombeck, C. T. (Abraham Lincoln Sch.
l., Chicago, Ill.). *Am. Surg.* 39(8):465-469,
73.

ndard lye burns were produced in 28 cats. No
tibiotic therapy was given. Treatment with β-
inopropionitrile (100 mg/kg/day, i.p.) was started
ediately in 12 cats and hydrocortisone sodium
cinate (10 mg/kg/day, i.p.), in 11 cats. A group
5 cats served as controls. Marked esophageal
enosis was seen in all animals 24 hr postburn, but
s resolved by 7 days. By the end of the second
k, the esophagus was almost completely stenotic
controls. All of these animals died around the
of the 3rd week of either inanition or aspira-
n. The animals in both treated groups maintained
ut a 50% esophageal lumen to the end of the study.
se treated with β-aminopropionitrile had a signi-
antly larger esophageal lumen than those treated
h the steroid. Values in these groups did not
nge from the 3rd to the 4th weeks postburn, in-
ating that stenosis did not progress after the
week. Animals treated with β-aminopropionitrile
t more weight than those receiving steroid
rapy, but the weight loss was not significant in
her of the treated groups. All the animals appeared
onically ill, but those receiving β-aminopropioni-
le were less lethargic. None of these cats
eloped either esophageal perforation or mediasti-
abscess. Given in doses which do not produce
er side effects, β-aminopropionitrile may be even
e effective than hydrocortisone.

6 PULMONARY COMPLICATIONS IN BENIGN ESOPHA-
GEAL DISEASE. *(E.)* Iverson, L. I. G.;
May, I. A.; Samson, P. C. (Samuel Merritt Hosp., Oakland, Calif.). *Am. J. Surg.* 126(2):223-228, 1973.

The cases of 400 patients with benign esophageal lesions were reviewed. The average age of the patients was 65 yr, with the majority between 55 and 75 yr. The type of esophageal disorders included hiatal hernia (372), achalasia (10), cricopharyngeal spasm (2), Zenker's diverticulum (6), primary stricture or web (5), presbyesophagus (1), benign tracheoesophageal fistula (1), motility disorder (1), recurrent cardiospasm (1), and collagen disease (1). Peptic ulcer occurred in 10% of the cases, and 5% had disease of the gallbladder, hypertension, and adult diabetes mellitus, resp. The most common pulmonary complication in hiatal hernia was pneumonia, which occurred in 11%. Bronchitis and changes on x-ray films occurred in 8% each. Episodes of aspiration were well documented in 4%. There was a 2% incidence of bronchiectasis. Pulmonary abscess was present in 1 case and resulted in death. When hiatal hernia is associated with reflux, esophagitis, or stricture, there is a significantly higher incidence of pulmonary complications (up to 56%). It is suggested that detailed investigation of the esophagus and swallowing mechanism be made in patients with chronic or recurrent inflammatory conditions of the lung and tracheobronchial tree. Pulmonary complications indicate that surgical repair of gastroesophageal reflux be undertaken, whether hiatal hernia is present or not.

6897 LONG-TERM RESULTS OF SURGICAL TREATMENT FOR BLEEDING OESOPHAGEAL VARICES IN CHILDREN WITH PORTAL HYPERTENSION. *(E.)* Keighley, M. R. B.; Girdwood, R. W.; Wooler, G. H.; Ionescu, M. I. (Gen. Infirm., Leeds, England). *Br. J. Surg.* 60(8): 641-646, 1973.

The long-term results of surgical treatment for bleeding esophageal varices in children with portal hypertension were studied in children (12 males and 12 females below 13 yr of age who presented with gastrointestinal bleeding. In 19 cases the initial presentation was unheralded gastrointestinal bleeding. Hepatosplenomegaly was present in 4 children, ascites in 1 and jaundice in 2. Etiology in these cases was as follows: cirrhosis (12) including portal cirrhosis, (5), congenital hepatic fibrosis(5), and postnecrotic scarring (2), extrahepatic obstruction (10) including splenic vein thrombosis (1), portal vein thrombosis (6), absent portal vein (3), and idiopathic (2). An atrial septal defect existed in 2 patients with congenital absence of the portal vein. Polycystic disease of both kidneys was found in 1 child with congenital hepatic fibrosis. Surgical treatment consisted of devascularizing procedures in 7 cases, splenectomy alone in 9, and shunts in 8. Though extrahepatic obstruction is considered to be associated with a better long-term prognosis than intrahepatic disease, the results of treatment in both groups were similar, with a 7-yr survival rate of 75%. Shunt surgery as a definitive procedure is advised in both groups, though the type of shunt used will depend on the age of the child and the site of obstruction.

6898 DYSFUNCTION OF THE LOWER ESOPHAGEAL SPHINCTER IN DISORDERS OTHER THAN ACHALASIA.

(E.) Kaye, M. D. (Univ. Colorado Med. Ctr., Denver). *Am. J. Dig. Dis.* 18(9):734-745, 1973.

High pressure dysfunction was studied in 9 patients (7 females and 2 males, aged 22-63 yr), all with symptoms of dysphagia and/or substernal chest pain. In 5, radiologic studies of the esophagus were normal, and in none was there an increase in esophageal caliber. Each patient had dysfunction of the lower esophageal sphincter, as assessed by manometry, the chief abnormality being impairment of relaxation in 7 and derangement of contraction in 2. All showed peristaltic activity in the esophageal body during manometric studies. The classic manometric pattern of diffuse esophageal spasm was present in 1 case. In the remainder, some of the manometric features of this disorder were present. These observations emphasize that the boundaries between achalasia, diffuse esophageal spasm, and other less well-characterized disorders of esophageal motility are blurred. Such disorders may represent parts of a continuous spectrum and may be etiologically related.

6899 GLYCOGENIC ACANTHOSIS OF THE ESOPHAGUS: A FORM OF BENIGN EPITHELIAL HYPERPLASIA.

(E.) Bender, M. D.; Allison, J.; Cuartas, F.; Montgomery, C. (VA Hosp., San Francisco, Calif). *Gastroenterology* 65(3):373-380, 1973.

Glycogenic acanthosis was studied in 5 male patients aged 54-65 yr. Typical endoscopic findings were white, raised, and round plaques, 2-5 mm in diameter, scattered throughout the esophagus and tending to occur on esophageal folds. Histologically, the plaques were characterized by focal areas of thickened squamous epithelium with increased numbers of cells that stained strongly for glycogen. Hyperkeratosis, cellular atypica, and dysplasia were absent. Four patients had either symptomatic acid reflux or distal esophagitis, but neither appeared incriminated in plaque formation. Although 4 patients had a history of chronic smoking and 2 were chronic alcoholics, there was no clear relation to smoking and alcohol abuse in these cases. Results suggest that glycogenic acanthosis is a benign esophageal lesion unrelated to leukoplakia or carcinoma. The etiology, pathogenesis, and natural history of the lesion remain to be determined.

6900 DEGLUTITION TACHYCARDIA.

(E.) Bajaj, S. C.; Ragaza, E. P.; Silva, H.; Goyal, R. K. (Hosp. St. Raphael, New Haven, Conn.). *Gastroenterology* 62(4):632-635, 1972.

A 45 yr old male physician had a 4 month history of paroxysmal atrial tachycardia associated with swallowing. He produced either a single premature atrial contraction or self-limiting atrial tachycardia, or atrial tachycardia with aberrant conduction, with each swallow. Balloon distention of the esophagus at the level of 25 cm from the incisors also produced similar arrhythmia. Treatment with procainamide (250 mg, 4 times/day) for a 3 week period abolished this deglutition tachycardia. He has remained asymptomatic for 1 1/2 yr.

6901 STIMULATION OF THE INCOMPETENT LOWER ESOPHAGEAL SPHINCTER. A POSSIBLE ADVANCE IN THERAPY OF HEARTBURN.

(E.) Farrell, R. L.; Roling, G. T.; Castell, D. O. (U.S. Naval Hosp., Philadelphia, Pa.). *Am. J. Dig. Dis.* 18(8):646-650, 1973.

The effect of hormonal and pharmacologic stimuli on lower esophageal sphincter pressure in 11 patients (5 females and 6 males; aged 25-72 yr) with symptomatic gastroesophageal reflux due to lower esophageal sphincter incompetence has been studied. Gastric alkalinization, pentagastrin (0.8 μg/kg, s.c.) edrophonium (10 mg, i.v.), and bethanecol (5 mg, s.c.) each resulted in marked increases in lower esophageal sphincter pressure. In all studies, pressure rose to a level occurring in normal subjects. Subsequently, all patients were given bethanecol (25 mg, p.o.) and pressure monitored for 2 hr. The lower esophageal sphincter pressure increased from a mean basal pressure of 5.6 mmHg to a peak of 16.9 mmHg at 50 min. Pressure remained elevated for the full 2 hr study. Both s.c. and p.o. bethanecol successfully increased lower esophageal sphincter pressure in all patients with symptomatic reflux to the level of resting pressure seen in normal subjects. These studies suggest a potential role for cholinergic agents in the therapy of symptomatic gastroesophageal reflux.

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(Fr.) Kron, B.; Vayre, P.; Debbasch, L. (Vaugirard Hosp., Paris, France). *Sem. Hop. Paris* 49(18):1268-1269, 1973.

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outh Africa). *S. Afr. Med. J.* 47(26):1137-
138, 1973.

904 PERFORATIONS AND RUPTURES OF THE
ESOPHAGUS. *(E.)* Lyons, W. S.; Seremetis,
. G.; De Guzman, V. C.; Peabody, Jr., J. W. (George-
own Univ. Sch. Med., Washington, D.C.). *Med. Ann.*
.C. 42(6):267-271, 1973.

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THE FOREGUT AND THEIR COMPLICATIONS.
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cotland). *Thorax* 28(4):424-428, 1973.

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S. *(E.)* Brain, R. H. F. (Guy's Hosp.,
ndon, England). *Thorax* 28(4):515-520, 1973.

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CARCINOMA WITH SARCOMATOID COMPONENT).
r.) Peloquin, A. B.; Vauclair, R. (Notre
me Hosp., Montreal, Canada). *Union Med. Can.*
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POLYCYSTIC KIDNEY AND LIVER DISEASE. *(E.)*
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rtz, C. (Hahnemann Med. Coll., Philadelphia,
). *N. Engl. J. Med.* 289(13):678-679, 1973.

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1973.

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TUBE. PROSPECTIVE STUDY. *(Sp.)*
omingo Varela, P.; Cosme, A.; Muro, J.; Cano,
.; Ortiz Vazquez, J. (Fac. Med., Free Univ.,
Madrid, Spain). *Rev. Esp. Enferm. Apar. Dig.*
39(3):283-298, 1973.

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6930 MODIFIED NISSEN FUNDOPLICATION AND THE "GAS-BLOAT" SYNDROME AS MEASURED BY THE INABILITY TO VOMIT. AN EXPERIMENTAL STUDY. *(E.)* Goldstein, R.; Butterfield, W. (Univ. Connecticut Med. Sch., Hartford). *Am. J. Surg.* 126(1):89-92, 1973.

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INTUBATION: A CASE REPORT. *(E.)* Peterson,
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6968 ACUTE STRIDOR IN ACHALASIA OF THE ESOPHAGUS (CARDIOSPASM). *(E.)* Giustra, P. E.; Killoran, P. J.; Wasgatt, W. N. (Knox County Gen. Hosp., Rockland, Maine). *Am. J. Gastroenterol.* 60(2):160-164, 1973.

6969 BARRET'S ULCER. *(Sp.)* Lopez Gallart, M.; Sebastia Vila, J. L. (Gallart-Mones Sch. Dig. Dis., Barcelona, Spain). *Rev. Esp. Enferm. Apar. Dig.* 39(6):731-734, 1973.

6970 STENOSING ESOPHAGITIS. *(Sp.)* Andreu Oller, L.; Sala Cladera, E. (no affil.). *Rev. Esp. Enferm. Apar. Dig.* 40(4):389-408, 1973.

6971 TRAUMATIC DIAPHRAGMATIC HERNIA WITH EVENTRATION OF THE LEFT DIAPHRAGM AND INTRATHORACIC GASTRIC VOLVULUS. *(Sp.)* Lopez Gallart, M.; Sebastia Vila, J. L. (Gallart-Mones Sch. Dig. Dis., Barcelona, Spain). *Rev. Esp. Enferm. Apar. Dig.* 40(2):213-218, 1973.

6972 GASTROESOPHAGEAL EROSINOS AND ULCERATIONS. EXPERIMENTAL STUDIES. *(E.)* Carrasquilla, C.; Weaver, A.; Amarasinghe, D. C.; Rota, A.; Walt, A. J.; Park, A. (Wayne State Univ. Sch. Med., Detroit, Mich.). *Arch. Surg.* 107(3):447-451, 1973.

6973 ESOPHAGEAL RECONSTRUCTION FOR STENOSIS DUE TO DIFFUSE SCLERODERMA. UTILIZING BLUNT DISSECTION OF ESOPHAGUS. *(E.)* Akiyama, H.; Kogure, T.; Itai, Y. (Toranomon Hosp., Tokyo, Japan). *Arch. Surg.* 107(3):470-472, 1973.

6974 LONG-TERM RESULTS OF OESOPHAGOPLASTY THROUGH THE RIGHT COLON. (CLINICAL, RADIOLOGICAL, CINERADIOGRAPHICAL AND MANOMETRIC EVALUATION). *(E.)* Latteri, S.; Deodato, G.; Russo, A.; Banna, P. (Inst. Thorac. Surg., Univ. Catania, Italy). *Chir. Gastroenterol.* 7(1):3-10, 1973.

6975 ENDOSCOPIC DIAGNOSIS OF SLIDING HIATUS HERNIA: STUDY OF 90 CASES. *(Sp.)* Perez Carnero, A.; Mino Fugarolas, G.; Jaramillo Esteban, J. L.; Muro, J. (La Paz Munic. Sanit., Madrid, Spain). *Rev. Esp. Enferm. Apar. Dig.* 40(1):23-34, 1973.

6976 EMERGENCY ESOPHAGEAL AND GASTRIC FIBROSCOPY IN 102 CASES OF UPPER GASTROINTESTINAL BLEEDING. *(Fr.)* Villand, J.; Carli, H.; Klepping, C. (no affil.). *Rev. Fr. Gastroenterol.* (87):77-84, 1973.

6977 DYSPHAGIA: GENERAL PRINCIPLES OF MANAGEMENT. *(E.)* McConchie, I. (Royal Melbourne Hosp., Australia). *Aust. N.Z. J. Surg.* 42(4):358-359, 1973.

6978 PEPTIC ESOPHAGEAL STENOSIS IN CHILDREN. *(E.)* Monereo, J.; Cortex, L.; Blesa, E. (Clin. Infantil "La Paz", Madrid, Spain). *J. Pediatr. Surg.* 8(4):475-478, 1973.

6979 PERORAL ESOPHAGEAL INTUBATION FOR OBSTRUCTIVE CARCINOMA OF THE ESOPHAGUS. *(E.)* Lewis, R. J.; Kunderman, P. J.; Sisler, G. E.; Mackenzie, J. W. (Rutgers Med. Sch., Brunswick, N.J.). *Ann. Thorac. Surg.* 16(2):148-161, 1973.

6980 GASTRIC VOLVULUS WITHIN A HIATUS HERNIA. A REPORT OF TWO CASES OF "UPSIDE-DOWN STOMACH". *(E.)* Yedinak, P. R. (no affil.). *Rocky Mt. Med. J.* 70(7):23-24, 1973.

6981 THE TREATMENT OF HEARTBURN AND OESOPHAGITIS. *(E.)* Hansky, J. (Prince Henry's Hosp., Melbourne, Australia). *Drugs* 5(5-6):446-452, 1973.

6982 SOME DIFFICULTIES IN THE TREATMENT OF DYSPHAGIA IN ADULTS. *(E.)* McConchie, I. (Roy. Melbourne Hosp., Australia). *Aust. N.Z. J. Surg.* 42(4):362-364, 1973.

6983 CARCINOSARCOMA OF THE ESOPHAGUS. CASE REPORT AND REVIEW OF THE LITERATURE. *(E.)* Calhoun, T.; Ali, S. D.; Muna, D.; Kurtz, L. H.; Simmons, R. L.; Nash, E. C. (Howard Univ., Washington, D.C.). *J. Thorac. Cardiovasc. Surg.* 66(2): 317-319, 1973.

6984 ADENOMAS OF THE ESOPHAGUS: A CASE REPORT AND REVIEW OF THE LITERATURE. *(E.)* Spin, F. P. (Dartmouth Med. Sch., Hanover, N.H.). *Gastrointest. Endosc.* 20(1):26-27, 1973.

6985 LOWER OESOPHAGEAL SPHINCTER AND PEPTIC OESOPHAGITIS. *(E.)* Ottenjann, R. (Munic. Hosp., Munich, Germany). *Acta Hepatogastroenterol.* 20(2):162-166, 1973.

See also, 6702, 6715, 6738, 6754, 6777, 6789, 6791, 6813, 6820, 6825, 6872, 7003, 7047, 8139, 8141, 8224.

STOMACH

6986 HISTOCHEMICAL STUDY OF MUCOPOLYSACCHARIDE IN GASTRIC CANCER. *(E.)* Hirose, S.; Yasutomi, M.; Murai, N.; Iwasa, Z.; Hirose, M.; Shindo, K.; Aso, R.; Kikkawa, N.; Razzaq, A. K. A. (Osaka Univ. Med. Sch., Japan). *Acta Histochem. Cytochem.* 5(3):153-160, 1972.

Mucopolysaccharide components of gastric cancers were examined histochemically. Mucoid cancer, signet cell cancer, and goblet cells of well-differentiated carcinoma showed a strong positive periodic acid Schiff (PAS) reaction and an extremely strong Mowry colloidal iron reaction. In alcian blue straining, signet cell cancer and goblet cells of well-differentiated carcinoma sometimes showed positive reaction. Stromata at the periphery of cancer infiltration were only weakly positive in the PAS reaction and in alcian blue staining, and no changes were observed after digestion tests. In contrast, a fairly strong colloidal iron reaction was observed n the stroma at the front of carcinoma. When etastasis to lymph node had occurred, reaction was een in the stroma around the cancer cells. After yaluronidase digestion, the stroma turned negative o collcidal iron reaction, regardless of whether esticular hyaluronidase or streptomyces hyaluroniase was applied. These results indicate that owry's colloidal iron reaction is the best of these staining methods for digestion tests of mucopolyaccharides. Most of the colloidal iron-positive ubstance is believed to be hyaluronic acid. Beond the infiltrating front of the gastric cancer, part of the substance is resistant to streptomyces yaluronidase digestion; this part is probably hondroitin sulfate.

987 THE CLINICAL SPECTRUM OF HEMORRHAGIC EROSIVE GASTRITIS. *(E.)* Dagradi, A. E.; Lee, E. R.; Bosco, D. L.; Stempien, S. J. (Dept. Med., Univ. California, Irvine). *Am. J. Gastroenterol.* 60(1):30-46, 1973.

Hemorrhagic "erosive" gastritis, diagnosed by gastroscopy during the phase of active bleeding, caused 117 patients (aged 28-83 yr) to be hospitalized on 159 occasions. In 90% of the admissions, ingestion of alcohol (51 patients) or salicylate-containing medications (26) alone, or in combination (29), caused the mucosal disorder. The ethanol-related group had histories of alcohol consumption ranging back to 40 yr. In some cases in the salicylate-related group, the drug was taken for less than 3 days. Medications ranged from plain aspirin to proprietary compounds. Rebleeding from hemorrhagic erosive gastritis occurred twice as frequently (30%) in the ethanol group as in the salicylate group (16%). Melena occurred in 26 admissions (6%), clinical shock in 77 (48%), and epigastric pain was greatest in those who ingested salicylates. Liver cirrhosis was demonstrated in 56 patients, including 70% of the ethanol group. Gastric ulcers occurred in 33% of the salicylate group, but in only 5% of the ethanol group. Peptic ulcers were active in 50% of the former group and 11% of the latter group. Emergency gastroscopic examination is the only nonsurgical method which can demonstrate the small superficial mucosal lesions of hemorrhagic gastritis. Surgery should be used only in cases where bleeding cannot be controlled by other means.

6988 QUALITATIVE AND QUANTITATIVE STUDIES OF ANTRAL AND FUNDIC G CELLS IN PERNICIOUS ANAEMIA. *(E.)* Polak, J. M.; Hoffbrand, A. V.; Reed, P. I.; Bloom, S.; Pearse, A. G. E. (Hammersmith Hosp., London, England). *Scand. J. Gastroenterol.* 31(3):361-367, 1973.

Samples of antral and fundic mucosa from 4 cases of pernicious anemia, 2 cases of atrophic gastritis, and 2 normal controls were examined by immunofluorescence and electron microscopy. Gross gastrin (G) cell hyperplasia was observed, by both techniques, in the pernicious anemia cases and the cells were found to be substantially degranulated. Presumptive G cells were commonly empty. Television image conversion analysis of the immunofluorescence preparations indicated gastrin levels/unit area at 4-5 times greater than normal. However, the true degree of G cell hyperplasia was not reflected by these figures. Comparisons between antral mucosa samples from pernicious anemia and from Zollinger-Ellison syndrome (Type 1), where the degree of hyperplasia of the fully granulated G cells may reach 30 X, indicated the true degree of hyperplasia as up to 50 X the normal value. These findings are in full agreement with the results of serum gastrin assay in pernicious anemia and demonstrate the value of parallel antral G cell and serum gastrin assays in elucidating the mechanisms of gastric acid secretion.

6989 ULTRASTRUCTURE OF THE GASTRIC MUCOSA IN ACHYLOUS (ATROPHIC) GASTRITIS. *(Rus.)*

Chkhetia, R. I.; Mikeladze, A. L. (State Inst. Postgrad. Med., Tbilisi, USSR). *Soobschch. Akad. Nauk Gruz. SSR* 68(2):457-460, 1972.

Electron microscope studies were made of fundal glands in aspiration biopsies from the stomachs of 10 patients with atrophic gastritis confirmed by functional, morphological, and histological criteria. In chief cells a marked decrease was observed in the electron density of the cytoplasm. Cisternae of the endoplasmic reticulum were disorganized and irregularly dilated. Similar changes were found in the apical part of the cell down to the cytoplasmic membrane which was smooth and had no villi. Occasional microtubules were found in the cytoplasm. Around the nuclei were dense groups of mucoid-like bodies. The number of ribosomes was decreased; none were present in large areas of the endoplasmatic membrane. The Golgi apparatus occupied a large area around the nucleus and consisted of small and large vesical-like cavities, some of which contained an osmophilic mass. Mitochondria were sometimes deformed with destruction of the cristae. Isolated microtubules and multivesicular bodies were occasionally found in the cytoplasm of parietal cells. The number of ribosomes and mitochondria was reduced. Microvilli were absent or small in the apical portion of the cell. Intracellular canaliculi were compressed, and somewhat thickened microvilli completely filled their lumens. In contrast to other findings reported in the literature, canaliculi were never dilated. It is suggested that these intracellular canaliculi may serve as a criterion for the functional evaluation of the state of parietal cells.

6990 INCIDENCE OF GASTRIC MALIGNANT NEOPLASMS IN THE POPULATION OF THE CITY OF WARSAW IN THE YEARS 1963-1968.

(E.) Gadomaska, H.; Koszarowski, T.; Karewicz, Z. (Inst. Oncol., Warsaw, Poland). *Pol. Med. J.* 11(6):1523-1530, 1972.

In a 6-yr period gastric neoplasms accounted for 16.1% of all malignant neoplasms in men in the Warsaw population. The incidence of gastric neoplasms was second only to pulmonary neoplasms. In women gastric neoplasms were in 4th place after neoplasms of the uterine cervix, breast, and liver and biliary tract; they accounted for 9.1% of all neoplasms in women. Gastric neoplasms accounted for 46.6% of all digestive tract neoplasms in men and 30.7% in women. Neoplasms in the liver, gallbladder, and biliary tract occurred twice as frequently in women as men. The mean patient age when gastric cancer was initially diagnosed was 59.4 yr in men and 63.7 yr in women. Confirmation was obtained histologically in 27.1% of the cases and radiologically in 10.5%. Surgery was performed in 27.9% of the cases. The incidence of gastric neoplasms as well as their frequency among all neoplasms do not show any tendency to increase, nevertheless they are a considerable danger to the population of Warsaw.

6991 SUPERFICIAL CANCER OF THE STOMACH: 41 CASES.

(Fr.) Moreaux, J.; Martin, E.; Mombet, J.; Housset, P.; Bloch, P. (Bichat Hosp., Paris, France). *Arch. Fr. Mal. App. Dig.* 61(12):711-724, 1972.

Superficial carcinomas, largely localized in the mucosa, were diagnosed in 41 patients (27 men and 14 women, aged 30-77 yr; mean age 56 yr). Single tumors were present in 37 patients and multiple tumors in 4. The tumor invaded only the mucosa in 22 patients, the muscularis mucosae in 15, and the tunica muscularis in 4; lymph node metastases occurred in 4 cases. All patients had epigastric pain before surgery, and half had attacks of epigastric pain characteristic of ulcers. Histories of epigastric pain dated back for more than 1 yr in 28 cases, and for more than 10 yr in 7 patients. Gastrointestinal bleeding occurred in 12 patients. Repeated stomach x-rays were suggestive of cancer in 28 cases, but 16 patients had radiological changes which were compatible with benign gastric ulcers and which disappeared after conservative treatment. Cancer was not diagnosed in any of the 11 patients examined with a rigid gastroscope, while diagnoses were established by biopsy in 12 of 14 patients examined with fibrogastroscopes. Neoplasms were located in the antrum in 40 cases and varied in area from 2 to 48 cm^2. Superficial gastric carcinomas were associated with simple gastric ulcers in 4 cases, an infiltrating carcinoma in 2 cases, gastritis and intestinal metaplasia of the antrum in 27 cases, and a leiomyoma in 1 case. In all but 2 cases, low partial gastrectomies were performed. None of the patients died postoperatively, and 36 are still alive. Three patients developed carcinomas of the gastric stump and died 18 months and 2 yr after surgery, resp.; the remaining patient was lost to follow-up. Two other patients died of intercurrent disease (diabetic coma and cerebral hemorrhage, resp.).

6992 DYNAMIC ASPECTS OF GASTRIC SECRETION ACCORDING TO THE GASTRIC ULCER STAGES USING PHENOL RED DILUTION METHOD. *(E.)* Misaki, F.; Kawai, K. (Kyoto Pref. Univ. Med., Japan). *Acta Hepatogastroenterol.* 20(4):343-351, 1973.

The phenol red dilution method was used with tetragastrin stimulation (4 μg/kg, s.c.) to reevaluate the relation between gastric acid secretion and peptic ulcer in 9 patients with duodenal ulcer, 31 with gastric ulcers, and 8 controls. Both basal and maximal acid outputs were lower in patients with gastric ulcers than in those with duodenal ulcers; the basal acid outputs of patients with gastric ulcers did not differ significantly from control values. Maximal acid output increased as gastric ulcers developed nearer to the duodenum. A correlation was found between acid output and the severity of atrophic gastritis. In duodenal ulcer both the basal secretion and response to tetragastrin were much greater than those in controls or in patients with gastric ulcers. The ratio of basal acid output to maximal acid output was high in duodenal ulcer, demonstrating a relative increase in basal secretion. No relation was found between acid secretion and the tendency of gastric ulcers to heal. In all but 2 patients, the basal acid output gradually decreased as gastric ulcers healed, but no change occurred in the maximal acid output. In 2 patients with intractable gastric ulcers the basal acid output increased progressively. These findings suggest that gastric acid secretion has a different effect on the treatment and healing of duodenal ulcers than it does in gastric ulcers.

6993 DETERMINATION OF THE INTRAGASTRIC LOSS OF ^{51}Cr ALBUMIN IN 7 CASES OF PROTEIN-LOSING GASTROPATHY. *(Fr.)* Vidon, N.; Crozatier, B.; ernier, J. J. (St. Lazare Hosp., Paris, France). *rch. Fr. Mal. App. Dig.* 62(3):201-209, 1973.

y using ^{51}Cr-labeled albumin, gastric clearance f albumin was determined in 7 patients (6 men and woman, aged 35-72 yr) with various types of gasritis (2 with Menetrier's disease, 3 with hypertrohic gastritis, and 1 each with ulcerative and atrohic gastritis). With one exception, all patients ad hypoalbuminemia (level < 35 g/liter). Under asal conditions these patients secreted a mean of .8 ml/hr albumin in gastric juice and after hisamine injection, a mean of 14.3 ml/hr; both of these alues are significantly higher than those found in ormal subjects (3.1 ml/hr and 2.6 ml/hr, resp.). he increase in gastric clearance of albumin was reater in patients with hypertrophic gastritis han in those with Menetrier's disease. A direct elation was found between albumin secreted in the astric juice and blood albumin levels in 1 patient n whom determinations were made during an exacer-ation and during a remission. The mean ^{51}Cr-abeled albumin excreted in the stools of these paients was less than 25 ml/24 hr, suggesting that ome albumin is absorbed in the gastrointestinal ract before it is excreted in the stools.

6994 FOOD DEPRIVATION, SHOCK STRESS AND STOMACH LESIONS IN THE RAT. *(E.)* Pare, W. P.; Temple, L. J. (VA Hosp., Perry Point, Md.). *Physiol. Behavior* 11(3):371-375, 1973.

The development of stomach lesions was studied in 140 male Sprague-Dawley rats deprived of food for 1-12 days. Weight loss amounted to 7% of the body weight for the first day and exceeded 30% by day 12. All rats developed rumenal ulcers after 5 days of fasting, but lesions of the glandular stomach were observed in only 7%. After 12 days of fasting, lesions in the body of the stomach had occurred in only 24% of the animals tested for that period. Another group of 120 male Sprague-Dawley rats were deprived of food for 1-5 days. Half of each sub-group was subjected to grid-shock stress consisting of a 5-sec 85 decibel tone followed by a 0.5 sec 0.5 milliamp scrambled grid shock. Tone-shock pairings were presented on a random VI 3-min schedule in effect 24 hr/day. Rats subjected to both fasting and stress lost more weight than animals which were only fasted. Ulcers of the glandular stomach occurred in only 2 rats in the fasting, no-stress group, and did not occur in any rats subjected to both fasting and stress. All other ulcers were rumenal ulcers. No significant difference was found between ulcer incidence in fasting no-stress and in fasting stressed groups for periods of 3, 4, or 5 days. These findings suggest that food deprivation, rather than stress, is the major factor contributing to the development of rumenal ulcers. Psychogenic factors are more likely to be involved in the development of ulcers in the glandular stomach.

6995 HISTOCHEMICAL STUDY OF SIALIC ACID IN GASTRIC TISSUE, MAINLY OF GASTRIC CANCER. *(E.)* Hirose, S.; Yasutomi, M.; Murai, N.; Iwasa, Z.; Hirose, M.; Shindo, K.; Aso, R.; Kikkawa, N.; Razzaq, A. K. A. (Osaka Univ. Med. Sch., Japan). *Acta Histochem. Cytochem.* 6(2):117-123, 1973.

A comparison was made between staining obtained with a modification of Bial's sialic acid reagent, developed by the authors, and the periodic acid-Schiff (PAS) reagent, alcian blue, and Mowry's colloidal iron stain on tissue from normal human stomach and from patients with stomach cancer and stomach ulcers. Both PAS and Bial's reagent reacted with different intensities with almost all cell structures in the stomach. In the normal stomach Bial's reagent stained chief cells in the fundic glands most intensely, while accessory and parietal cells were stained lightly. Fairly intense staining occurred in the muscularis and serosa, but connective tissue was stained lightly. Paneth cells remained negative. Almost no reaction occurred in pyloric glands of the normal stomach, but fairly strong reactions occurred in the protoplasm and at the striated border in intestinal metaplasia. The reaction was most intense, particularly at the tips of cells, both at loci of intestinal metaplasia and where proliferative changes were present. Bial's reaction was more intense in immature than in mature regenerating cells around the edges of ulcers. Within the cell, Bial's reaction occurred primarily in the protoplasm but very weakly in the paraplasm; goblet cell mucus was very lightly stained. Regardless of the histological type of cancer, sialic acid staining was generally weaker in cancer tissue than in the muscularis mucosae or fundic glands. Despite the weak reaction of surrounding cancer cells, fairly strong reactions occurred in exsudate inside the lumen of highly differentiated adenocarcinomas or in necrotic material at the center of cancer foci. Moderately intense reactions occurred in highly differentiated cancer cells with striated borders. The protoplasm of signet cell cancers reacted weakly and vacuoles were entirely negative. Connective tissue surrounding cancer cells stained more intensely than the cancer cells themselves. The other staining reagents all reacted with goblet cell mucus in highly differentiated cancers and the vacuoles of signet cells cancer, whereas Bial's reagent did not. These findings suggest that sialic acid may play a role in cell proliferation under some conditions and that increases in the sialic acid content of cancer cells observed in previous biochemical studies may be a reflection of a high concentration of sialic acid in exsudate and/or stroma.

6996 PROGNOSIS FOR CARCINOMA OF THE STOMACH.

(E.) Hoerr, S. O. (Cleveland Clin. Fdn. Ohio). *Surg. Gynecol. Obstet.* 137(2):205-209, 1973.

In a series of 478 patients with histologically verified carcinoma of the stomach, 46% were considered acceptable for resection for cure. Overall postoperative fatality was 10.2%. Among gastric resection patients the mortality was 10.3%. No deaths occurred in the 37 patients under 50 yr of age who underwent curative resection. The rate of 5-year survivors was 3 times greater in those requiring only simple, partial gastrectomy for curative resection as compared to those requiring total gastrectomy or esophagogastrectomy. Survival rate was also 3 times greater in the group whose lymph nodes were unaffected. Of the 72 5-year survivors, 9 had proven or probable recurrent carcinoma. Survival rate was independent of the patient's sex. It is felt that the policy followed in this series of using small operative procedures for small cancers and extensive operative procedures for large cancers is equal in effectiveness to those policies calling for extensive resection in small cases.

6997 BLOOD SEROTONIN AND LIVER FUNCTION IN PATIENTS WITH GASTRIC CANCER.

(Rus.) Agaev, I. N. (Sci. Res. Inst. Roentgenol., Radiol., Oncol., Baku, USSR). *Vopr. Onkol.* 19(6):38-41, 1973.

Blood serotonin levels, BSP retention, and serum protein fractions were measured in 78 patients (51 men and 27 women, aged 34-78 yr) with stomach cancer and in 19 normal controls. Blood serotonin levels were significantly higher in patients with gastric cancer (mean 0.215 ± 0.098 μg/ml) than in controls (0.096 ± 0.055 μg/ml). Mean serotonin levels were significantly higher in patients with stage IV cancer than in those with stage II and III cancer: these values were 140.3% and 90%, resp. of control values. Mean BSP retention was significantly higher (11.7 ± 5.82%) in patients with stage IV cancer than in those with stage II and III cancer (7.6 ± 4.13%). Patients with stomach cancer had significantly lower serum albumin levels and significantly higher α_1- and α_2-globulin levels than normal subjects; γ-globulin levels tended to increase in cancer patients. The most pronounced changes in serum protein fractions were observed in patients with generalized metastases. These findings suggest that there may be a relation between serotonin and globulin values in patients with gastric cancer.

6998 BILE REFLUX GASTRITIS. DIAGNOSIS, MEDICAL AND SURGICAL THERAPY.

(E.) Scudamore, H. H.; Eckstam, E. D.; Fencil, W. J.; Jaramillo, C. A. (The Monroe Clin., Wis.). *Am. J. Gastroenterol.* 60(1):9-22, 1973.

Bile reflux gastritis was studied in 42 patients (22 females and 20 males, aged 25-75 yr). No gastric surgery had ever been performed on 23 of the 42 patients; vagotomy and pyloroplasty had been performed on 7. Vagotomy and antrectomy or hemigastrectomy were performed with Billroth I in 2 and with Billroth II in 9. Diaphragmatic hernia repair alone was made in 1 and in conjunction with one of the above operations in 6 other patients. Cholecystectomy had been performed in 18 and 4 had evidence of gallbladder disease. Severe, unrelenting epigastric pain existed in all 42 patients. Other symptoms included nausea (16), gas (13), weight loss (10), anorexia (10), diarrhea (0), heartburn (7), sour eructation (5), dumping syndrome (4), dysphagia (3), and anemia or vitamin B_{12} deficiency (4). Diagnosis was made by gastroscopic examination and the demonstration of bile reflux at gastroscopy or during gastric analysis and confirmed by gastric biopsy and ancillary findings on upper gastrointestinal x-rays. Cholestyramine (initially 4 g 1 hr after meals and at bedtime) usually brought response in 1 or 2 weeks but was continued for several months. The main side effect was constipation which was easily controlled. For severely ill patients, a modified Roux-en-Y anastomosis was created in which the biliary branch of the Y was anastomosed to the jejunum 50 to 60 cm distal to the gastrojejunal anastomosis. The main complication following this procedure was gastric retention or difficulty in evacuation of the stomach contents.

6999 HISTOLOGY OF GASTRIC CARCINOMA OCCURRING AFTER GASTRIC SURGERY FOR BENIGN CONDITIONS.

(E.) Taksdal, S.; Stalsberg, H. (Rikshospital, Oslo, Norway). *Cancer* 32(1):162-166, 1973.

In 84 patients (67 males and 17 females, ages covering the twenties through the eighties) with gastric cancer who had previously undergone gastric surgery for benign conditions, histological classifications were made according to Lauren's method and these were compared to gastric cancers in patients with no previous gastric surgery. Apart from the absence of sarcomas among the previously operated patients, there was little difference in the distribution of histologic types among patients. However, in previously operated males, the proportion of intestinal-type tumors did not show the expected increase with age. Nor was there an increase in intestinal-to-diffuse ratio that might have been expected from the location of the tumors and from the association between duodenal ulcer and blood groups and between blood groups and tumor histology. It is concluded that the incidence of intestinal and diffuse types of gastric carcinoma both increase after gastric surgery, but the increase appears to be larger for the diffuse type. Intestinal metaplasia and gastritis were no more prominent in sections from the primary resectates from 16 patients who later developed gastric cancer than in controls. Leukocyte infiltration was more pronounced in carcinomas of postoperative patients than in carcinomas found in patients who had not undergone gastric surgery. The surgical technique employed in the initial operation had no appreciable effect on the distribution of histologic types among the gastric carcinomas that did develop later. The lack of association between histological changes in the gastric mucosa after the first resection and subsequent development of gastric cancer supports the hypothesis that postoperative gastric cancer results primarily from surgery and not from the disease for which the operation was performed.

7000 CHARACTERISTICS OF CYTOLOGICAL FINDINGS ON ASPIRATION BIOPSIES FROM PATIENTS WITH CHRONIC GASTRITIS.

(Rus.) Kliukina, L. B. (Sci. Res. Inst. Oncol. Med. Radiol., Minsk, USSR). *Vopr. Onkol.* 19(3):43-48, 1973.

An analysis was made of histological and cytological findings on aspiration biopsies taken from the stomachs of 121 patients with chronic gastritis, 43 of whom were referred with a diagnosis of stomach cancer. The gastric mucosa was normal in 15 patients, while 54 had superficial gastritis, 11 had chronic nonatrophic gastritis, 17 had chronic atrophic gastritis, 20 had chronic atrophic "regenerating" gastritis, and 4 had atrophic hyperplastic gastritis. Decreased gastric secretion was associated with different variants of atrophic gastritis in 37 of 65 patients and with superficial gastritis in 22. In contrast to subjects with normal gastric mucosa, patients with superficial gastritis had a larger number of inflammatory cells, histiocytes capable of phagocytosis, plasma cells and lymphoreticular cells in smears made from biopsied material. Superficial cells were multi- or isoprismatic, round, and had small cytoplasmic vacuoles. In 45 patients the nuclei were monomorphic and contained small homogeneous chromatin granules. In 9 of these patients the nuclei were hypertrophic, the ratio of nucleus/cytoplasm was abnormal, chromatin was irregularly distributed, the ratio of nucleus/cytoplasm was abnormal, chromatin was irregularly distributed, and many large nucleoli were present. Similar findings were observed in patients with chronic nonatrophic gastritis, but lymphocytes and plasma cells were the most common inflammatory cells and groups of cells with moderately hypertrophic hyperchromic nuclei contained many nucleoli covering an area of 2-2.5 μ^2 or a few large nucleoli covering an area of 4μ^2. Cellular atypism was more pronounced in biopsied material from chronic atrophic "regenerating" gastritis and atrophic hyperplastic gastritis with the most common signs being cytoplasmic basophilia, abnormalities in the ratio of nucleus/cytoplasm, and masses of bare giant cells. Highly significant differences were found for the mean values of cell and nuclear area and the mean ratio of nucleus/cytoplasm between these patients and those in the other groups. Signs of intestinal metaplasia were detected in 20 of these patients.

7001 THE EFFECT OF GASTRIC ANTIGENS ON THE IN VITRO MIGRATION OF LEUCOCYTES FROM PATIENTS WITH ATROPHIC GASTRITIS AND PERNICIOUS ANAEMIA.

(E.) Goldstone, A. H.; Calder, E. A.; Barnes, E. W.; Irvine, W. J. (Roy. Infirm., Edinburgh, Scotland). *Clin. Exp. Immunol.* 14(4):501-508, 1973.

The leucocyte migration test was used to study delayed hypersensitivity to gastric antigens in patients with pernicious anemia (18), atrophic gastritis and achlorhydria but without pernicious anemia (10), and control subjects (14). The percentage of pernicious anemia patients showing inhibition of migration in the presence of a crude extract of gastric mucosa, liver mitochondria, stomach mitochondria, and stomach microsomes was 50, 55, 50, and 50%, resp. The results in atrophic gastritis were 0, 20, 20, and 0%, resp., and those in the control subjects were 0, 14, 7, and 14% resp. A significant difference between pernicious anemia patients and controls occurred with all 4 antigens. There was a significant difference using crude extract and stomach mitochondria and microsomes between pernicious anemia patients and atrophic gastritis but not with liver mitochondria. No significant difference occurred between atrophic gastritis and controls although the results tended to be midway between pernicious anemia values and controls. These results suggest that cell-mediated immunity is more strongly implicated in pernicious anemia than it is in atrophic gastritis which has not progressed to pernicious anemia.

7002 PROGNOSIS IN GASTRIC LYMPHOMA.

(E.) Hoerr, S. O.; McCormack, L. J.; Hertzer, N. R. (Cleveland Clin. Fdn., Ohio). *Arch. Surg.* 107(2):155-158, 1973.

Gastric lymphoma was reviewed in 44 patients (30 males and 14 females, aged 24-71 yr) operated on during a 22 yr period. The disease appeared to originate in the stomach in 39 of these patients. The types of gastric lymphoma present in this series included lymphocytic lymphoma (5), histiocytic lymphoma (20), mixed lymphocytic and histiocytic lymphoma (18), and plasmacytoma (1). A resection of varying extent was undertaken for cure in 16. Only 2 have died of lymphoma and there are 10 five-yr survivors to date. There are no 5-yr survivors in 24 patients whose disease was beyond surgical cure, irrespective of treatment. There are 2 five-yr survivors in a group of 4 whose lesion could have been resected but who received, for various reasons, irradiation as the definitive treatment. Prognosis in gastric lymphoma is twice as good as in gastric carcinoma. Subclassification of lymphoma had no practical value in this small series.

7003 MORPHOLOGICAL CHARACTERISTICS OF THE ESOPHAGEAL MUCOSA IN CHRONIC GASTRITIS AND STOMACH CANCER. *(Rus.)*

Aleksandrova, N. M.; Inshakov, L. N. (Kazakh Sci. Res. Inst. Oncol. Radiol., Alma-Ata, USSR). *Vopr. Onkol.* 19(6):31-34, 1973.

Endoscopic and histological examinations were made of the esophageal mucosa in 74 patients with various forms of gastritis, 1 with a gastric polyp undergoing malignant transformation and associated with atrophic gastritis, and 25 with stomach cancer. These patients included 36 women and 64 men; 74.6% were natives of Kazakhstan. Common pathological changes in the esophageal mucosa included leukoplakia (48.3%), epithelial hyperplasia (20.8%), and chronic esophagitis (14.2%). In 9 patients leukoplakia was associated with early signs of malignant transformation. Pathological changes, particularly leukoplakia, were found most frequently in patients with atrophic gastritis (53.5%) and stomach cancer (22.5%). An association of 2 or more pathological processes was observed in the esophageal mucosa of 20.2% of these patients; in particular, leukoplakia occurred in combination with chronic esophagitis and dysplasia.

7004 EFFECT OF CIGARETTE SMOKING ON COMPETENCE OF THE PYLORUS: PRELIMINARY STUDY. *(E.)*

Read, N. W.; Grech, P. (Northern Gen. Hosp., Sheffield, England). *Br. Med. J.* 3(5875):313-316, 1973.

The competence of the pylorus was studied in 13 normal volunteers (8 males and 5 females, aged 20-67 yr) and 9 dyspeptic patients (6 males and 3 females, aged 29-64 yr) by means of a radiological technique involving intubation of the duodenum. Of the dyspeptic patients, 1 had chronic duodenal ulcer and another had gastric ulcer. Epigastric pain or discomfort was present in all 9 patients. The pylorus was competent in most normal individuals and in fewer than half of the dyspeptic patients. However, on smoking a cigarette, appreciable increase in duodenogastric reflux was seen in 9 of the 13 normal volunteers and in 7 of the 9 dyspeptic patients. Such induced pyloric incompetence and the resultant damage to gastric mucosa by bile entering the stomach may explain the increased incidence of gastritis and gastric ulceration in heavy smokers.

7005 THE EFFECT OF GASTRIC COOLING ON HEMOSTASIS.

(E.) Waterman, N. G.; Walker, J. L. (Univ. Louisville Sch. Med., Ky.). *Surg. Gynecol. Obstet.* 137(1):80-82, 1973.

The effect of gastric cooling on hemostasis was studied in 7 adult dogs. Gastric irrigation continuously for 30 min with iced saline solution lowered the recorded stomach temperature to 20 C. Results show that gastric cooling simulating clinical practice causes a 3-fold increase in stomach wall bleeding time. Both the prothrombin and clotting times, done at the same lower temperature, also were significantly increased. The adverse effect on the bleeding times was not counteracted by a 50% reduction in blood flow.

7006 ULTRASTRUCTURE OF PARIETAL AND CHIEF CELLS OF THE STOMACH IN ATROPHIC GASTRITIS. *(Rus.)*

Salupere, V. P.; Kiarner, Iu. K. (Central Lab. Med. Res., Tartu Univ., USSR). *Arkh. Patol.* 34(10):20-25, 1973.

An electron microscope study was made of secretory cells in biopsy material obtained from the gastric fundus of 11 patients with chronic atrophic gastritis and of 3 normal controls. All of these patients had histamine-resistent achlorhydria or hypochlorhydria. Ultrastructural changes observed in parietal cells included a considerable decrease in the number of mitochondria and mitochondrial cristae. These cristae were shortened and located at the periphery of the mitochondria, while the centers of the mitochondria remained empty. These ultrastructural changes were essentially the same in patients with and without antibodies to parietal cells, and the size of the mitochondria did not differ from the size of those found in controls. Changes in the chief cells were less pronounced, but these cells appeared to have fewer zymogen granules than those in controls. It is suggested that the decrease in the number of mitochondria and ultrastructural changes in mitochondria found in atrophic gastritis are manifestations of a disturbance in the energy metabolism in parietal cells and of a decrease in phosphorylation necessary for hydrochloric acid production.

7007 CELL ALTERATIONS OF THE GASTRIC MUCOSA IN BENIGN DISEASES AND MALIGNANT TUMORS. *(E.)*

Martuzzi, M. (G. B. Morgani Hosp., Forli, Italy). *Pathol. Eur.* 7(3-4):263-272, 1972.

Histological sections were studied from 100 gastric carcinomas, 20 peptic ulcers, 20 gastrites, and 5 polyps. Smears of gastric washings studied came from 20 gastric carcinomas, 20 ulcers, 20 gastrites and 5 polyps. Where carcinoma was present, a significant increase in cells with telophasic and interphasic nuclei was associated with decreased numbers of cells with early prophasic nuclei. The nuclear/cytoplasmic ratio, the nucleolar/nuclear ratio, and the degree of chromasia were significantly greater than in areas with benign lesions. The entire gland of the gastric mucosa may present alterations when a tumor is present. In mucosal areas close to cancer, the nuclear structures may resemble nuclei of the malignant tumor. Prominent nuclear alterations leading to the interpretation of "malignancy-associated changes" were observed in either mucosal epithelial cells or stromal cells of areas concurrent with gastric lesions in 79% of the carcinoma cases as compared to 16% of the cases with benign lesions. These results indicate that changes other than just atrophic gastritis and polyps have an increased incidence in people suffering from carcinoma. The changes reported here are thought to occur from alterations in the reproductive and maturative functions of cells. It is suggested that these alterations may represent steps in the development of the cancer.

7008 MICROPOLYPOUS GASTRITIS: ITS NEOPLASTIC POTENTIAL. *(Sp.)* Rodriguez Olleros, A.; Taveras, J. E. (Fac. Pharm., Univ. Puerto Rico, San Juan). *Bol. Assoc. Med. P.R.* 65(2):37-42, 1973.

7009 HISTOCHEMICAL STUDY OF MUCINS IN EXPERIMENTAL ATROPHIC GASTRITIS IN THE DOG. *(Fr.)* Casteleyn, P. P. (no affil.). *C. R. Soc. Biol. (Paris)* 167(3/4):591-593, 1973.

7010 TREATMENT OF HODGKIN'S DISEASE OF THE STOMACH. *(Ger.)* Hoffken, K.; Hornung, G.; Bruntsch, U.; Becker, G.; Schmidt, C. G. (Essen Clin., Ruhr Univ., Germany). *Dtsch. Med. Wochenschr.* 98:148-152, 1973.

7011 SO-CALLED EARLY GASTRIC CANCER AND ITS DETECTION. *(E.)* Stadelmann, O.; Miederer, S. E.; Loffler, A.; Muller, R.; Kaufer, C.; Elster, K. (Med. Clin. Univ., Bonn, Germany). *Endoscopy* 5(2):70-76, 1973.

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7014 PREDNISOLONE THERAPY FOR PATIENTS WITH GASTRITIS AND SECRETORY INSUFFICIENCY. *(Rus.)* Radbil', O. S.; Khaletova, S. S. (V. I. Lenin State Inst. Postgrad. Med., Kazan, USSR). *Kazan. Med. Zh.* (5):33-34, 1972.

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7017 CONSEQUENCES OF GASTRIC RESECTION AND VAGOTOMY. *(E.)* Silen, W. (Harvard Med. Sch., Boston, Mass.). *Mayo Clin. Proc.* 48(9): 653-655, 1973.

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7084 TOTAL GASTRECTOMY. *(E.)* Kortas, J.; Duda, S. (Med. Acad., Szczecin, Poland). *Pol. Med. J.* 9(6):1539-1543, 1972.

7085 THE EFFECT OF GASTRECTOMY, PERFORMED FOR CANCER, ON THE HEPATIC FUNCTION. *(Rus.)* Tsekhanovich, T. I.; Tikhonova, N. M. (State Med. Inst., Tomsk, USSR). *Vopr. Onkol.* 18(10):31-35, 1972.

7086 INVASION OF THE STOMACH BY MACROFOLLICULAR LYMPHOBLASTOMA. *(Ger.)* Kissling, U.; Escher, J.; Clmencon, G. (Buergersp., Solothurn, Switzerland). *Helv. Med. Acta* 36(2/3):207-208, 1972.

7087 51 CASES OF CARCINOMA OF THE STOMACH. *(Fr.)* Mouchet, A.; Marquand, J.; Guivarch, M.; Saglier, Mme.; Godquin, B.; Ben Hamida, M. F. (Ctr. Med. Surg. Foch, Paris, France). *J. Chir. (Paris)* 104(5):373-386, 1972.

7088 ULCERATING SUPERFICIAL GASTRIC ADENOCARCINOMA PRESENTING WITH MASSIVE UPPER GASTROINTESTINAL HEMORRHAGE. *(E.)* Munsell, W. P. Oklahoma City Clin., Oklahoma City). *J. Okla. State Med. Assoc.* 66(5):193-197, 1973.

See also, 6327, 6430, 6722, 6724, 6735, 6738, 6744, 6747, 6754, 6757, 6762, 6763, 6780, 6804, 6806, 6813, 6814, 6819, 6820, 6830, 6833, 6834, 6847, 6852, 6862, 6865, 6866, 6872, 6880, 6902, 6916, 6931, 6967, 6971, 6972, 6976, 6980, 7110, 7115, 7162, 7165, 7199, 7200, 7251, 7500, 7993, 8088, 8092, 8100, 8149, 8153, 8203, 8224.

STOMACH

Peptic Ulcers

7089 TREATMENT OF CHRONIC GASTRIC ULCER WITH CARBENOXOLONE AND GEFARNATE: A COMPARATIVE TRIAL. *(E.)* Langman, M. J. S.; Knapp, D. R.; Wakley, E. J. (Univ. Nottingham Med. Sch., England). *Br. Med. J.* 5871(3):84-86, 1973.

Chronic gastric ulcer in 68 patients (49 males and 19 females) was treated in an outpatient clinical trial with either carbenoxalone (100 mg, 3 times/day) or gefarnate (50, 100, or 200 mg, 4 times/day). All treatments were of 4 weeks duration. Ulcer healing was consistently greater during carbenoxalone treatment. One third of the patients receiving carbenoxalone gained weight rapidly and unexpectedly, and were given diuretic treatment, compared with 2 of the 12 patients receiving the highest dose of gefarnate, neither of whom developed clinical edema.

7090 MANAGEMENT OF ACUTE STRESS ULCER AFTER CARDIAC SURGERY. *(E.)* Taylor, P. C.; Loop, F. D.; Hermann, R. E. (Cleveland Clin. Fdn., Ohio). *Ann. Surg.* 178(1):1-5, 1973.

In 12 of the 38 patients who developed stress ulcers after cardiac surgery, gastrointestinal bleeding subsided after intensive medical treatment that included iced saline lavage, fresh whole blood transfusions, and administration of antacid solutions, tranquilizers, and Vitamin K. The remaining 26 patients required surgical intervention for control of massive hemorrhage or perforation. Vagotomy and pyloroplasty with oversewing of the bleeding ulcers stopped the bleeding and controlled the ulcer diathesis in the majority of patients. Only 2 of 19 patients who underwent vagotomy and pyloroplasty rerequired reoperation for recurrent bleeding; gastric resection was reserved for these patients and for 5 who had an unusually severe erosive process. Althoug mortality was not higher among the gastric resection patients (2/7), the results support the belief that conservative operations are indicated in temporary stress-provoking situations. Recurrent bleeding was factor in only 1 of the 8 deaths in the present series. The other deaths were due to cardiovascular or pulmonary complications.

7091 HYPOXIA AND STRESS ULVER FORMATION IN THE RAT. *(E.)* Mullane, J. F.; Smith, J. C.; Wilfong, R. G. (Walter Reed Army Inst. Res., Washington, D.C.). *Surgery* 74(3):326-332, 1973.

The effects of hypoxemia, anemia, and changes in gastric circulation on the development of gastric lesions have been evaluated in rats subjected to 7 hr of restraint stress. Rats were exposed to 10% O_2 for 7, 14, and 50 hr and to 7% O_2 for 7 hr. Anemia was produced acutely by the double exchange of blood for Plasmalyte solution. Gastric circulatory changes were produced by the injection of epinephrine (1.0 mg/kg, i.p.). Hypoxemia (10% O_2; Pa_{O_2} 36 mm Hg) for 7, 14, and 50 hr had no effect on gastric lesions with restraint stress. When the severity of hypoxemia was increased (7 hr of 7% O_2; Pa_{O_2} 27 mm Hg) there was an increased number of gastric erosions with restraint. Acute anemia (hematocrit 18%) without hypoxemia and with 7 hr of hypoxemia (10% O_2) protected the gastric mucosa against the development of gastric erosions induced by restraint stress. Epinephrine did not increase the incidence of gastric lesions of rats that breathed ambient air but did increase the number of erosions when 10% O_2 was substituted for air. Hypoxia alone is not a major cause of gastric lesions with stress, but hypoxemia combined with altered gastric circulation might produce a degree of hypoxia in the stomach critical for the development of gastric lesions.

7092 THE EFFECT OF INSULIN HYPOGLYCAEMIA ON SERUM GASTRIN AND GASTRIC ACID IN NORMAL SUBJECTS AND PATIENTS WITH DUODENAL ULCER. *(E.)*

Cowley, D. J.; Baron, J. H.; Hansky, J.; Korman, M. G. (Roy. Postgrad. Med. Sch., London, England). *Br. J. Surg.* 60(6):438-443, 1973.

Serum gastrin was measured by radio-immunoassay in 11 normal subjects (10 males and 1 female, mean age 34 yr) and in 17 patients (15 males and 2 females, mean age 39 yr) with duodenal ulcer during insulin hypoglycemia with and without concomitant aspiration of gastric acid. Insulin hypoglycemia alone caused a rise in serum gastrin from 8.0 to 45.0 pg/ml in patients with duodenal ulcer, which was significantly greater than the rise from 13.0 to 29.0 pg/ml in controls. During gastric aspiration serum-gastrin levels remained elevated for longer periods. An almost complete discrimination between patients with duodenal ulcer and normal subjects was provided by the maximum increase of serum gastrin after insulin during gastric aspiration. When serum gastrin was measured during insulin hypoglycemia combined with intragastric neutralization of acid, the discrimination between the 2 groups was complete. The timing of the peak serum gastrin and the lowest blood-glucose coincided, but the peak acid output occurred 15-30 min later. Serum gastrin was inversely correlated with blood-glucose. Blood-glucose decreased to significantly lower levels in unaspirated than in aspirated subjects. It is suggested that patients with duodenal ulcer produce more gastrin than normal subjects in response to insulin hypoglycemia (and, by inference, to vagal stimulation). This supports the concept of increased functional G-cell mass in duodenal ulcer patients, and indicates the physiological roles of vagally released gastrin and of the acid inhibitory mechanism. Discriminant functions observed in the study could form the basis of tests for the presence of the duodenal ulcer diathesis.

7093 DIAGNOSIS AND TREATMENT OF TROPHIC ULCERS OF THE STOMACH. *(Sp.)*

Meeroff, M.; Segal, J. E.; Meeroff, J. C. (Metropolitan Sanitorium, Buenos Aires, Argentina). *Rev. Esp. Enferm. Apar. Dig.* 39(2):187-210, 1973.

In a 6-year period trophic ulcers of the stomach were diagnosed in 96 patients (73 men and 23 women). Ulcers had recurred once in 18 patients, twice in 14, and more than twice in 3. Massive bleeding occurred in 12 cases. The gastric lesion was located in the upper vertical 1/3 of the lesser curvature in 15, in the middle 1/3 in 48, and in the lower 1/3 in 30 patients; it was found on the posterior surface in 3 patients. Ulcers were large in 38 and moderately large or small in 58. Maximal gastric acid output, measured after histamine stimulation in 64 patients, was 4-8 mEq/hr in 51, 8-10 mEq/hr in 12, and 10-12 mEq/hr in 1. The most common causes of trophic ulcer were senile degeneration with evidence of arteriosclerosis (31 cases), malnutrition (10), emotional factors or stress (10), and systemic infections (9). Other causes included senile degeneration without arteriosclerosis (2), arteriosclerosis and malnutrition (4), reducing diets (5), corticosteroids (4), amphetamines (2), amphetamines and reducing diets (2), multiple trauma (3), surgery (6), cirrhosis with hyperchlorhydria (6), and emphysema (2). Most patients responded to conservative therapy consisting of diet, rest, drugs (anti-inflammatory agents, gefarnate, colloidal alumina, and bismuth), and measures directed at eliminating the underlying cause. Surgery was performed for massive bleeding (6 patients), suspected malignancy which was not confirmed (3), ulcer recurrence (3), and failure of medical therapy (6).

7094 THE NORMAL PYLORIC WALL AND CHANGES IN ITS PROPORTIONS IN "ANTRAL DISEASE": A MORPHOLOGICAL CONTRIBUTION TO STOMACH ULCER. *(Ger.)*

Liebermann-Meffert, D.; Allgower, M. (Munic. Hosp., Basel, Switzerland). *Z. Gastroenterol.* 10(7):535-542, 1972.

A morphological study was made of the antrum and pylorus in 18 kidney donors, aged 13-61 yr, with no evidence of stomach disease and in 72 patients, aged 20-80 yr, who had undergone gastrectomy for stomach ulcer. Regardless of the site of the ulcer and its depth, the relief of the folds and mucosa was flattened in the entire stomach, and particularly in the antrum, of patients with stomach ulcer. The submucosa was edematous. In some cases the transverse pyloric fold was thickened and flattened, mucosal prolapse was present, and the musculature was thicker than normal. In 8 of the 72 stomachs from ulcer patients the pylorus could not be dilated because the pyloric muscle was indurated with connective tissue and looked like a cord which constricted the lumen. Regardless of the site of the ulcer, the thickness of the antral and/or pyloric walls was increased to different degrees in all ulcer patients. Variations in the thickness of the walls were more pronounced in ulcer patients than in controls. These findings suggest that changes in the thickness of tne antral and pyloric walls are involved in the pathogenesis of stomach ulcers.

7095 THE INACTIVATION BY CARBENOXOLONE OF INDIVIDUAL HUMAN PEPSINOGENS AND PEPSINS. *(E.)*

Roberts, N. B.; Taylor, W. H. (United Liverpool Hosp., England). *Clin. Sci. Mol. Med.* 45(2):213-224, 1973.

Swine pepsin A and human pepsins 1, 3 and 5 are inhibited by carbenoxolone, in suspension at pH 4.0. Human pepsin 5 is the most readily inhibited, and human pepsin 1 the least. Inhibition occurs by a time-dependent, temperature-dependent process which is proportional to the quantity of carbenoxolone suspended. Carbenoxolone solution at pH 7.4 and pH 8.0 inhibits the activation of the total pepsinogens of human gastric mucosal extracts and of the individual pepsinogens 1, 3 and 5. Pepsinogen 1 was the most readily inhibited, pepsinogen 5 the least. Chymotrypsin was readily inhibited by carbenoxolone at pH 7.4 and 8.0. Trypsin was not inhibited at pH 7.4 but was relatively weakly inhibited at pH 8.0. Pronase was weakly inhibited at pH 7.4 and 8.0, but papain was weakly activated. Carbenoxolone therefore inhibits enzymes (pepsins and chymotrypsin) which split proteins at the same bonds, rather than for enzymes with similar active centres (chymotrypsin and trypsin). The results suggest that, *in vivo*, carbenoxolone might diminish peptic activity in 3 ways: by inactivating pepsinogens irreversibly in the mucosal cells or at some point before their activation to pepsins; by inhibiting pepsins irreversibly in the gastric lumen; and by binding pepsins in the lumen without destroying their activity but decreasing their effective concentration. These results support the hypothesis that pepsins, in particular pepsin 1, are factors in the etiology of peptic ulcer.

7096 CORRELATION OF MUCOSAL HISTOLOGY AND ASPIRIN INTAKE IN CHRONIC GASTRIC ULCER.

(E.) MacDonald, W. C. (Dept. Med., Univ. British Columbia, Vancouver, Canada). *Gastroenterology* 65(3):381-389, 1973.

The microscopic appearance of the mucosa of 50 partial gastrectomy and 1 vagatomy and pyloroplasty specimens in cases of chronic gastric ulcer was correlated with the patient's intake of aspirin. Multiple sections were examined from 10 to 15 tissue blocks representing all areas of each specimen. The pyloric gland mucosa was abnormal in the specimens of 44 partial gastrectomy patients, 8 of whom habitually used aspirin. Of the ulcers, 42 were on the lesser curve or posterior wall, including the 8 in aspirin users. The pyloric gland mucosa was essentially normal in 6 gastrectomy specimens and around the locally excised ulcer. Ulceration of normal mucosa involved the greater curve of the antrum in 5 of the 7 patients. All 7 patients with normal pyloric gland mucosa habitually used aspirin. The stomachs of 2 who took indomethacin or phenylbutazone as well as aspirin were identical with those of patients who only took aspirin or aspirin-phenacetin-caffeine tablets. The normal pyloric gland mucosa and the unusual distribution of the ulcers in these 7 patients suggest that the ulcers were drug-induced. The identical appearance of the stomachs of 2 patients taking known ulcerogenic drugs and aspirin with those of patients taking aspirin or aspirin-phenacetin-caffeine tablets alone suggests that the latter are also ulcerogenic.

7097 VAGOTOMY AND HEALING OF PHENYLBUTAZONE ULCER IN THE RAT.

(E.) Kairaluoma, M. I.; Larmi, T. K. I. (Dept. Surg., Univ. Oulu, Finland). *Scand. J. Gastroenterol.* 31(3):313-316, 1973.

Ulcers were induced in 210 male Sprague-Dawley rats by i.m. injection of phenylbutazone (200 mg/kg). The ulcers healed very fast; one-third epithelialized in 12 hr, half the number in 72 hr, and all in 6 days. Healing was faster in very superficial ulcers than in those which penetrated deeper or were more extensive. Despite the discontinuation of acid secretion it caused, vagotomy, which had been performed on 105 of the 210 rats, slightly retarded the healing process; however, the difference between groups was not statistically significant. Healing peptic ulcers did not affect the animals' weight gain, whereas vagotomy retarded it significantly. This, together with antral stasis, might explain why vagotomy did not promote ulcer healing.

7098 RESPONSE TO PENTAGASTRIN IN MAN. II. SECRETION OF ACID.

(E.) Wormsley, K. G. (Maryfield Hosp., Dundee, Scotland). *Acta Hepatogastroenterol. (Stuttg.)* 20(2):150-158, 1973.

The patterns of secretion of acid in response to continuous infusion of pentagastrin (0.06 to 6.0 μg/kg/hr, i.v.) were studied in 145 healthy subjects and 123 patients with duodenal ulcer and gastric ulcer. The concentration of acid is independent of the rate of secretion if stimulation is near maximal, but is lower, relative to secretory rate, if the secretory stimulus is weak or if the gastric mucosa is abnormal. Similarly, the relation between the output of acid and the rate of secretion depends on whether onset, or steady rates, of stimulation are considered and whether the gastric mucosa is normal or abnormal. It is concluded that the relation between the secretion of acid and rate of secretion by the stomach is complex, and care must be taken to avoid analyses based on pooled data derived during different stages or intensities of stimulation or from subjects with differing gastric mucosa. It is suggested that abnormal secretion in response to pentagastrin is indeed a qualitative difference from the normal response and not a statistically lower limit of normal. Normal stomachs stimulated with pentagastrin secreted high concentrations of acid is in response to all degrees of stimulation and cannot be made to secrete abnormally. Conversely, abnormal stomachs cannot be made to achieve high acid concentrations, even with supramaximal doses of pentagastrin.

7099 HISTOLOGICAL CHANGES IN THE GASTRIC MUCOSA OF CHRONIC GASTRIC ULCER PATIENTS TREATED

WITH CARBENOXOLONE. *(E.)* Thomas, E.; Hall, P.; Hislop, I. G. (Queen Elizabeth Hosp., Woodville, Australia). *Gut* 14(7):552-554, 1973.

Of 25 patients with chronic lesser curve gastric ulcer, 15 (12 males and 3 females, aged 35-70 yr) were treated with carbenoxolone (100 mg, 3 times/day for 3-8 weeks. Coexistent cardiac, hepatic, or hypertensive disease precluded carbenoxolone therapy in 10 patients (4 males and 6 females, aged 40-70 yr). Gastroscopic examination at 3-8 weeks showed complete healing in 11 of the 15 patients treated with carbenoxolone and in 8 of the 10 not so treated. Chronic gastritis was present in both proximal and distal direct-vision mucosal biopsies in 24 patients. In the proximal biopsy, chronic superficial gastritis was noted in 21 cases and chronic atrophic gastritis in 3 cases. In the distal biopsy, chronic superficial gastritis was observed in 23 patients and chronic atrophic gastritis in 1. Gastritis persisted in all patients despite therapy. In subsequent 'blind' assessment of the biopsies at 3-8 weeks and on follow-up, it was impossible to tell which patient had received carbenoxolone or whether the ulcer had healed. Similarly, study of mononuclear cell infiltration of the lamina propria failed to indicate which patients had received the drug. Since the morphological changes in the gastric mucosa persist unaltered even under the influence of a drug that promotes healing, the relation between gastritis and gastric ulcer is uncertain.

7100 PHENYLBUTAZONE ULCER AND VAGOTOMY IN THE RAT. *(E.)* Larmi, T. K. I.; Kairaluoma, M. I. (Dept. Surg., Univ. Oulu, Finland). *Scand. J. Gastroenterol.* 31(3):307-311, 1973.

Intramuscular injection of 200 mg/kg phenylbutzone produced glandular ulcers without mortality in 90% of 60 male Sprague-Dawley rats. When the dose was raised to 250 mg/kg, i.m., in 20 rats, the mortality rate was 35% and all surviving animals developed ulcers. Ulcer formation correlated with the duration of phenylbutazone action, the incidence and severity of ulcers increasing as a function of time during the 6 hr observation period. Ulcers appeared in the corpus part of the stomach 1 hr after drug injection and 2 hr later in the antrum. The incidence of ulcers was highest in the corpus part, where the ulcer crater was always covered by a digested blood coagulum. Antral ulcers did not penetrate below the mucosal surface. Vagotomy just before phenylbutazone injection completely inhibited ulcer formation, and none of the 20 vagotomized animals died within 6 hr of the injection. While animals vagotomized 1 week earlier had a reduced ulcer incidence (5.9%), 16 of the 17 died of toxic effects within 6 hr of phenylbutazone injection. It is suggested that the ulcerogenic action of phenylbutazone is possible not by direct local erosion through the mucosa.

7101 ACID SECRETION IN PATIENTS WITH A PERFORATED DUODENAL ULCER. *(E.)* Mason, M. C.; Brennan, T. G.; Giles, G. R. (St. James Hosp., Leeds, England). *Scand. J. Gastroenterol.* 8(5):421-424, 1973.

Maximal gastric acid secretion has been measured in a consecutive series of 42 patients with perforated duodenal ulcers. It was significantly higher than normal levels both in the 25 patients (23 males and 2 females, aged 20-62 yr) who had a history of chronic dyspepsia prior to the perforation and in those 17 (14 males and 3 females, aged 17-80 yr) who had few, if any previous symptoms. The mean basal secretion in patients with perforation of an acute ulcer was 5.3 mEq/hr, compared to 5.8 and 5.6 mEq/Hr for patients with perforated and uncomplicated chronic duodenal ulcer, resp. The normal mean basal secretion in control subjects was 2.4 mEq/hr. The mean maximal acid output in patients with uncomplicated chronic ulcers was 40.1 mEq/hr, compared to 35.3 mEq/hr for perforated acute ulcers, 35.3 mEq/hr for perforated chronic ulcers, and 21.6 mEq/hr for normal subjects. The long-term prognosis following simple suture of the perforation was good in the cases of acute perforations but poor if there had been prolonged preoperative dyspepsia. This prognosis was not related to the levels of acid secretion.

7102 PYLORIC REFLUX AND THE HEALING OF GASTRIC ULCERS. *(E.)* Cocking, J. B.; Grech, P. (Isle of Thanet Dist. Hosp., Ramsgate, England). *Gut* 14(7):555-557, 1973.

A study was made of 10 patients (4 males and 6 females, average age 53 yr) with benign gastric ulcer situated in the middle third of the lesser curve. All were outpatients and received carbenoxolone sodium (50 mg, 3 times/day) and antacids as therapy. In 3 additional patients the ulcers were complicated by chronic duodenal ulcers (2) and a radiographical deformity of the antrum due to scarring (1). All gastric ulcer patients had marked or moderate pyloric reflux in the erect position before treatment. After healing of the ulcers, 8 patients had only mild reflux when erect, and in 2 cases the pylorus had become competent. In the 2 patients with chronic duodenal ulcers, reflux diminished but the pylorus did not become competent in either case. In the patient with pyloric scarring, marked reflux in the erect position still was present, but the mild reflux which had been occurring in the supine position was gone. Thus the healing of a gastric ulcer is associated with a lessening of the duodeno-gastric reflux. Smoking was performed by 40% of those patients in this study and was discouraged during treatment. It is suggested that duodeno-gastric reflux may be an important step in the pathogenesis of gastric ulceration.

7103 PERFORATED GASTRIC ULCER. *(E.)* Rees, J. R.; Thorbjarnarson, B. (McKay-Dee Hosp. Ctr., Ogden, Utah). *Am. J. Surg.* 126(1):93-101, 1973.

Among 51 patients (40 males and 11 females, aged 19-80 yr) with perforated gastric ulcers encountered over a 37 yr period, 22 had perforated acute and 29 had chronic ulcers. Of these 51 patients, 12 had malignant lesions and 4 had collagen vascular diseases. Other diseases included carcinomas of the rectum (2), pancreas (1), and kidney (1); multiple myeloma (1); Hodgkin's disease (2); systemic lupus erythematosus (2); rheumatoid arthritis with portal vein thrombosis (1); periarteritis nodosa (1); and postnecrotic cirrhosis (1). All 11 patients who received conservative therapy alone died. Plication of the ulcer was the initial treatment in 37. In 3 others resection was carried out. Further complications of gastric ulcer accounted for 5 of 9 operative deaths. A more aggressive approach to the poor risk patient may be indicated, as these patients may withstand 1 surgical procedure well, but not additional ones. It is suggested that patients surviving plication or a perforated gastric ulcer be advised to undergo resection at a later date.

7104 EFFECT OF TRUNCAL VAGOTOMY ON THE INCREASE IN GASTRIC ACID SECRETION INDUCED BY SMALL BOWEL RESECTION IN DOGS.

(E.) Buxton, B.; Wasunna, A. E. O.; Saunders, J.; Gillespie, I. E. (Western Infirm., Glasgow, Scotland). *Digestion* 8(4):293-298, 1973.

The effect of truncal vagotomy on gastric hypersecretion induced by extensive small bowel resection has been studied in dogs with vagally innervated gastric pouches. Resection of 75% of the small bowel resulted in a 45% increase of the daily acid collection. Truncal vagotomy after small bowel resection did not alter the acid output. Small bowel resection caused a significant decrease in acid secretion 2 hr after a meal. By 5-6 hr, a significant increase in secretion had occurred. Resection caused no change in the total acid response for the 6 hr period following the meal. Truncal vagotomy after small bowel resection resulted in a 47% reduction in the total acid output for the 6 hr period following the meal, but did not reduce the delayed part of the acid response or the increase in the 24 hr acid output. Thus, truncal vagotomy is not effective in blocking the mechanism by which small bowel resection results in an increased acid output. After truncal vagotomy there was no change in parietal cell responsiveness to pentagastrin (1-8 μg/kg/hr, i.v.). Complications after truncal vagotomy included transient diarrhea and weight loss in 2 dogs. These findings suggest that selective gastric vagotomy may be preferred over truncal vagotomy.

7105 GASTRIN, AGE, AND THE GASTRIC MUCOSA.

(E.) Stricland, R. G.; Korman, M. G.; Hansky, J. (Walter and Eliza Hall Inst. Med. Res., Melbourne, Australia). *Aust. N.Z. J. Med.* 3(2):152-156, 1973.

The relation of serum gastrin levels to age was studied in 120 patients (84 men and 36 women, aged 22-93 yr). These consisted of: (1) 29 patients with intact gastric mucosa with normal gastric acid secretion who were seronegative for parietal cell antibody; (2) 64 with atrophic gastritis and achlorhydria who were seropositive for parietal cell antibody; and (3) 27 with atrophic gastritis and achlorhydria who were seronegative for parietal cell antibody. Serum gastrin levels, which ranged from 0-100 pg/ml in group (1), were increased in 59 of 64 patients (92%) in group (2) and in 3 of the 27 (11%) in group (3). An age-related change in serum gastrin levels was observed in group (2) but not in groups (1) or (3). Thus, the previously reported increase in serum gastrin with age in random hospital populations is due to a subgroup with atrophic gastritis who are predominantly seropositive for parietal cell antibody rather than to a general age-related change in the gastric mucosa.

7106 ALTERATIONS IN PYLORO-DUODENAL JUNCTION FOLLOWING VAGOTOMY AND PYLOROPLASTY.

(E.) Bertheussen, K. J.; Faber, B.; Svendsen, K. (Central Hosp., Naestved, Denmark). *Acta Radiol. Diag.* 14(3):273-277, 1973.

Total abdominal vagotomy and Weinberg pyloroplasty were employed in the treatment of duodenal ulcers in 65 patients (55 men and 10 women). Of these 65, 43 also had gastrostomies with drainage and feeding tubes. Ulceration was demonstrated prior to operation in 55 patients and some deformation of the duodenal bulb was evident in 5. Following operation 24% of those patients without gastric retention had developed grade I retention and 1 had grade II retention. Surgery relieved retention in 2 of the 10 patients with grade I; in 2 other patients, retention progressed to grade II. Thus, one effect of the operation was increased delay in gastric emptying, but this did not seem clinically significant in this selected group of individuals. No relation was established between the roentgenologic and insulin test results. Familiarity with post-pyloroplasty appearances of the pylorus region is essential in the roentgenologic assessment of patients with possible recurrent ulceration, as emphasized by the fact that 30 patients in this study were reported as still having ulceration postoperatively, although none was operated on for recurrence and confirmation of these reports is lacking.

7107 DIVERGENT NATURE OF GASTRIC MUCOSAL PERMEABILITY AND GASTRIC ACID SECRETION IN SICK PATIENTS WITH GENERAL SURGICAL AND NEUROSURGICAL DISEASE.

(E.) Gordon, M. J.; Skillman, J. J.; Zervas, N. T.; Silen, W. (Harvard Med. Sch., Boston, Mass.). *Ann. Surg.* 178(3):285-294, 1973.

Changes in gastric mucosal permeability and gastric acid secretion were assessed in 13 patients (5 males and 8 females, aged 19-78 yr) with general surgical illnesses and in 9 patients (7 males and 2 females, aged 23-74 yr) with diseases of the central nervous system by using an acid-free NaCl-LiCl technique. Gastric mucosal permeability and gastric acid secretion were estimated by the change in the ratio of $\Delta(\text{Li}^+/\text{polyethylene glycol})$ and $\Delta(\text{H}^+/\text{polyethylene glycol})$, resp. Gastric mucosal permeability was normal in 6 and increased in 7 acutely ill general surgical patients. Hypotension, sepsis, respiratory failure, renal insufficiency, jaundice, and death occurred more frequently in the group with increased gastric mucosal permeability. Gastric mucosal permeability was normal in all 9 neurosurgical patients, but gastric acid secretion was significantly higher than in the group of general surgical patients with increased gastric mucosal permeability and decreased acid secretion. Gastric bleeding occurred prior to study in 10 of 22 patients. Gastric mucosal permeability was increased in 4 of the 5 neurosurgical patients who bled and in all of the 5 general surgical patients who bled; gastric acid and pepsin secretion were also increased in the former group. Clinical complications were significantly more frequent in patients who bled. These investigations provide evidence for a relation between increased gastric mucosal permeability and gastric bleeding. Patients with neurological injuries complicated by hypotension and respiratory failure may develop the same kind of ulceration seen in general surgical patients. It is suggested that classical Cushing's ulceration of the deeply penetrating or perforating variety is a distinctly different clinical entity.

7108 FIVE YEAR FOLLOW-UP RESULTS OF OPERATIONS FOR DUODENAL ULCER.

(E.) Postlethwait, R. W. (no affil.). *Surg. Gynecol. Obstet.* 137(3): 387-392, 1973.

In elective operations for duodenal ulcer, performed on 1357 male patients, the type of operation was randomized, but the type of drainage or reconstruction was not. Follow-up data obtained at 5 yr showed the following postoperative mortality rates and rates for recurrent ulcers: vagotomy and drainage 0.6% and 6.2%, resp.; vagotomy and antrectomy 0.9% and 0.7%, resp.; vagotomy and hemigastrectomy 0.6% and 0.9%, resp.; and gastrectomy alone 1.8% and 3.7%, resp. Late related deaths occurred in 10 cases. The differences between postoperative and late related deaths were not significant for the 4 types of operations performed. Unrelated deaths, most of which were due to cardiovascular diseases or malignancies, were significantly less common among patients who received vagotomy and hemigastrectomy than among those given other types of operations. Recurrences were significantly more frequent after pyloroplasty than after gastrojejunostomy and were most common after gastroduodenostomy, except after gastric resection. These findings indicate that truncal vagotomy and resection of the distal part of the stomach best protect the patient from recurrent ulcer. After 5 yr, patients who had larger amounts of their stomach removed required less ulcer medication, but these patients developed early satiety or small pouch syndrome and anemia more readily than those with less extensive gastrectomies.

7109 SELECTION OF OPERATION FOR DUODENAL ULCER BASED ON ACID SECRETORY STUDIES--A REAPPRAISAL.

(E.) Robbs, J. V.; Bank, S.; Marks, I. N.; Louw, J. H. (Groote Schuur Hosp., Cape Town, South Africa). *Br. J. Surg.* 60(8):601-605, 1973.

Recurrent duodenal or jejunal ulceration was assessed 5-10 yr following selective surgery for duodenal ulceration in 253 patients after vagotomy and drainage and in 55 patients after vagotomy and antrectomy. In the vagotomy and drainage group 8.6% developed proven or highly suspected recurrent duodenal or jejunal ulcer. None had preoperative maximal acid output values less than 25 mEq/r No recurrent jejunal ulcers occurred in the vagotomy and antrectomy group even though they had the same incidence of incomplete vagotomy by Hollander's criteria as the vagotomy and drainage group. It is suggested that patient selection for vagotomy and drainage be based on a preoperative maximal acid output of 25 mEq/hr as opposed to the previously used level of 40-50 mEq/hr. Vagotomy and antrectomy should be employed if the maximal acid output is greater than 25 mEq/rhr.

7110 THE EFFECT OF VAGOTOMY ON THE INHIBITION OF GASTRIC SECRETION BY INTRADUODENAL FAT.

(E.) Ward, A. S. (Queen Elizabeth Hosp., London, England). *Br. J. Surg.* 60(7):533-536, 1973.

Pentagastrin-stimulated gastric secretion was measured in 13 patients before and after infusion of a peanut oil emulsion into the distal duodenum. Acid outputs were measured in 6 nonoperated patients with duodenal ulcers; in 6 patients following a minimum of 6 months after truncal vagotomy and pyloroplasty for duodenal ulcer, and in 1 patient before and after surgery. The completeness of vagotomy was confirmed in all vagotomized patients by the Hollander test. Infusion of fat into the duodenum caused a highly significant decrease in gastric secretion in both vagotomized and nonvagotomized patients. The latent period and duration of inhibition were also similar, suggesting that the underlying mechanism is the same. Inhibition of gastric secretion was due solely to a volume effect since the acid concentrations remained unchanged after duodenal fat infusion. Almost complete inhibition of gastric secretion in vagotomized patients makes it unlikely that a vagal component is involved in the mechanism of this response. A vagal component cannot be ruled out completely in nonoperated patients since the absolute changes produced by fat infusion are so much greater in this group than in vagotomized patients. These results suggest that there is little advantage in preserving the nerve supply to the duodenum at vagotomy since inhibition of gastric secretion by intraduodenal fat is apparently mediated by a nonvagal mechanism in man.

7111 ACID SECRETION IN RELATION TO RECURRENCE OF DUODENAL ULCER AFTER VAGOTOMY AND DRAINAGE.

(E.) Cowley, D. J.; Spencer, J.; Baron, J. H. (Roy. Postgrad. Med. Sch., London, England). *Br. J. Surg.* 60(7):517-522, 1973.

Acid secretory responses of 24 patients (19 males and 5 females) with recurrent ulcer after vagotomy and drainage were retrospectively compared with those of 25 patients (23 males and 2 females) with a positive insulin test but no recurrent ulcer and with those of patients with a negative insulin test. Patients with recurrent ulcer were an average of 10 years younger at the time of the initial operation than patients with an incomplete vagotomy but no recurrence, although their pre- and postoperative acid secretory responses were similar. Insulin tests were unreliable when performed less than 3 months after vagotomy. The only possible criterion for prediction of recurrent ulceration was a postoperative reduction of less than 60% in the peak acid output after pentagastrin. Equal numbers of patients with early and late positive responses to insulin developed a recurrent ulcer. It is suggested that routine postoperative insulin tests may be helpful in assessing the efficiency of the vagotomist but are of limited prognostic value. The value of postoperative insulin tests lies in the diagnostic evaluation of postvagotomy dyspepsia.

7112 ONE HUNDRED PATIENTS FIVE YEARS AFTER SELECTIVE GASTRIC VAGOTOMY AND DRAINAGE FOR DUODENAL ULCER.

(E.) Amdrup, E.; Jensen, H. E. (Munic. Hosp., Copenhagen, Denmark). *Surgery* 74(3):321-325, 1973.

Of 134 patients who underwent selective gastric vagotomy and pyloroplasty for duodenal ulcer, 12 died during follow-up. Causes of death were cardiopulmonary or thromboembolic disease (9), pre-existing cirrhosis (1), rectal cancer (1), and gastric cancer (1). Of the original 134, 100 (11 females and 89 males, aged 41 to over 60 yr) submitted to follow-up examination 5 yr after surgery. Of these 100, 6 had recurrent ulcers; 5 had gastric retention resulting from inadequate or scarred pyloroplasty. Ulcers were located in the antrum (2, insulin test late positive), in the duodenum (2, insulin test negative) and at the antrum-duodenum junction (2, 1 insulin test negative, 1 late positive). All of these patients became asymptomatic after antrectomy. All other patients in this series were cured of ulcer symptoms by selective vagotomy and pyloroplasty. Moderate dumping occurred in 27% of the patients and was severe in 5 and incapacitating in 2; 14 patients had looser stools than before operation. Incapacitating diarrhea occurred in 1 patient several years after the operation. The results of surgery were considered excellent in 85%, good in 5%, and failures in 10%. Failures included severe dumping, severe diarrhea, and recurrent ulcer. At 2 to 4 months following operation, insulin test was negative in 79%, late positive in 16%, and early positive in 5%. In 62 patients, the test was repeated after 5 years, showing the same distribution. In 77%, the result was stable compared to the early insulin test; in 13%, a negative test became late positive; and in 10%, a positive test became negative.

7113 OBSERVATIONS ON THE SURFACE ARCHITECTURE OF HISTAMINE-INDUCED GASTRIC ULCERATIONS IN THE GUINEA PIG.

(E.) Poulsen, S. S. (Anat. Dept., Univ. Copenhagen, Denmark). *Acta Pathol. Microbiol. Scand.* [*A*], 81(8):483-497, 1973.

Gastric ulcerations were induced in adult male guinea pigs by daily injection of a slowly absorbed histamine preparation (12 mg/kg, i.m.) for up to 18 days. The ulcerogenic action was rendered as constant and gentle as possible so that the various stages of the ulceration process could be studied thoroughly. Therefore, the animals were not fasted before or during the experiment, and they were protected from the acute musculovascular effect of histamine by a low dose of promethazine (2 mg/kg, i.m.) prior to each injection of histamine. In the course of the first 5 days numerous superficial erosions appeared, but true ulcers which penetrated the lamina muscularis mucosae did not form until the 5th-10th day. At the end of 10 days a number of the superficial erosions had regenerated. After 18 days the tendency to form new erosions had decreased, and many of the superficial erosions had regenerated. Stereomicroscopic examination after periodic acid-Schiff staining of whole mounts showed the individual ulcerations standing out distinctly as pale, sharply defined structures on a deep purple background.

7114 DUODENOCHOLEDOCAL FISTULA AS A COMPLICATION OF PEPTIC ULCER. *(Sp.)* Monte Albelda, F.; Herrero Bernabeu, C. (La Fe Munic. Sanit., Valencia, Spain). *Rev. Esp. Enferm. Apar. Dig.* 40(1):93-102, 1973.

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7186 GASTRIC MOTILITY DURING EXPERIMENTALLY INDUCED CONFLICTS IN SUBJECTS WITH STOMACH DISEASE. *(It.)* Lanfranchi, G. A.; Trombini, G.; Bortolotti, M.; Miglioli, M.; Stegagno, L. (Inst. Med. Pathol. I, Univ. Bologna, Italy). *Boll. Soc. Ital. Biol. Sper.* 48(21):738-741, 1972.

7187 BLOOD PRESSURE AND PEPTIC ULCER. *(Fr.)* Goulis, G.; Sakellaridis, D.; Sidiropoulos, E.; Concouris, L. (Hippokrateion Hosp., Thessaloniki Hosp., Greece). *Arch. Fr. Mal. App. Dig.* 61(12): 745-748, 1972.

7188 ULTRASTRUCTURAL CHANGES IN THE LIVER OF PATIENTS WITH PEPTIC ULCER FOLLOWING STOMACH RESECTION. *(Rus.)* Etyrska, M. (Reg. Hosp., Stara Zagora, Bulgaria). *Arkh. Patol.* 34(10):56-59, 1972.

7189 PROGNOSTIC VALUE OF THE HISTALOG TEST IN DUODENAL ULCERS. *(Fr.)* Rheault, M. J.; Tetreault, L. (Hotel Dieu Montreal, Canada). *Union Med. Can.* 102(5):1043-1048, 1973.

7190 ON THE EFFECT OF SELECTIVE PROXIMAL VAGOTOMY ON THE PARIETAL CELLS IN GASTRIC ULCERS. *(E.)* Holle, G.; Fellner, K.; Schauer, A. (Surg. Polyclin., Univ. Munich, Germany). *Chir. Gastroenterol.* 7(1):35-50, 1973.

7191 THERAPEUTIC TRIALS IN PEPTIC ULCER. OUT-PATIENT TREATMENT OF DUODENAL ULCER BY PENTAMETHYL-TETRA-HYDROPYRIDINE-HCl (PTH). *(E.)* Gutz, H. J.; Berndt, H. (Central Inst. Cancer Res., Acad. Sci., Berlin, Germany). *Acta Hepatogastroenterol.* 20(3):242-247, 1973.

7192 VAGOTOMY AND PYLOROPLASTY IN THE TREATMENT OF GASTRODUODENAL ULCER COMPLICATIONS. *(Ger.)* Hell, K.; Schuman, L.; Schultheiss, H. R.; Allgower, M. (Surg. Dept., Univ. Basel, Switzerland). *Dtsch. Med. Wochenschr.* 98(22):1104-1108, 1973.

7193 THE FATE OF 165 CASES OF BLEEDING PEPTIC ULCER TREATED ON A SPECIALISED INTENSIVE CARE UNIT. *(Fr.)* Conte, M.; Jarrousse, P. (St. Antoine Hosp., Paris, France). *Sem. Hop. Paris* 49(8):545-547, 1973.

7194 GASTRIC ULCER. CORRELATION BETWEEN ENDOSCOPY, CLINICAL FEATURES, AND RADIOLOGY. *(Sp.)* de La Revilla, L.; Marti, J.; Martin-Vivaldi, R.; Fernandez, A.; Torres, J. M. (Ruiz de Alda Sanit., Granada, Spain). *Rev. Esp. Enferm. Apar. Dig.* 39(6):661-674, 1973.

7195 A REVIEW OF SURGICAL THERAPY FOR PEPTIC ULCER DISEASE: 1942-1968. *(E.)* Fratkin, L. B. (no afill.). *Am. Surg.* 39(8):470-474, 1973.

7196 VAGAL CONTROL OF HISTAMINE-STIMULATED GASTRIC ACID SECRETION. *(E.)* Hall, W. H.; Hodges, S. C. (VA Hosp., Oklahoma City, Okla.). *Am. J. Dig. Dis.* 18(9):801-802, 1973.

7197 EFFECTS OF PROPANTHELINE BROMIDE AND MILK PLUS CHEESE ON HEALING OF CHRONIC GASTRIC ULCERS IN RATS. *(E.)* Okabe, S.; Pfeiffer, C. J. (Presbyterian Univ. Pennsylvania Med. Ctr., Philadelphia). *Am. J. Dig. Dis.* 18(9):746-750, 1973.

7198 CIRCULATING GASTRIN IN PEPTIC ULCER DISEASE. *(E.)* Walsh, J. H.; Grossman, M. I. (VA Wadsworth Hosp. Ctr., Los Angeles, Calif.). *Mt. Sinai J. Med.* 40(3):374-381, 1973.

7199 PRIMARY CANCER OF THE GASTRIC STUMP. *(Sp.)* Berenguer, J.; Soto, J. M.; Belda, A.; Gonzalez-Vara, P.; Rayon, J. M. (La Fe Munic. Sanit., Valencia, Spain). *Rev. Esp. Enferm. Apar. Dig.* 40(4):369-370, 1973.

7200 STUDY OF TOTAL PROTEINS IN GASTRIC JUICE WITH THE LOWRY METHOD IN NORMAL SUBJECTS AND PATIENTS WITH VARIOUS STOMACH DISEASES. *(Sp.)* Rodrigo Gomez, J. M.; Aparisi Quereda, L.; Blanes Masson, F.; Serra Desfilis, M. A.; Guix Garcia, J.; Tomas Ridocci, M.; Parrilla Paricio, P. (Fac. Med., Valencia, Spain). *Rev. Esp. Enferm. Apar. Dig.* 40(1):1-16, 1973.

See also, 6387, 6402, 6404, 6698, 6737, 6748, 6752, 6776, 6778, 6779, 6811, 6847, 6858, 6865, 6878, 6893, 7007, 7032, 7036, 7206, 7219, 7582, 8027, 8028.

7201 THE DUODENAL MICROFLORA IN RELATION TO VARIOUS SYMPTOMS AND MANIFESTATIONS IN PATIENTS WITH EXTRAHEPATIC BILIARY DISEASE. *(E.)*

Engstrom, J.; Hellstrom, K. (Serafimer Hosp., Stockholm, Sweden). *Acta Med. Scand.* 193(4):267-272, 1973.

This study comprised 39 patients with cholelithiasis and/or chronic cholecystitis and 54 patients who had previously been cholecystectomized. Of the non-cholecystectomized patients, choledocholithiasis was observed in 6, and stenosis of the common bile duct in 1. Of the cholecystectomized patients, 4 had choledocholithiasis, 2 choledochoduodenostomy and 1 stenosis of the common bile duct. Duodenal aspirates from 23 of the patients (class 1) contained more than 10^3 of aerobic colonic microorganisms per ml. No growth or less than 10^3 of such organisms and less than 10^5 of common pharyngeal species per ml of the aspirate (a "normal" microflora, class 2) was encountered in 48 cases. A pharyngeal flora, defined as more than 10^5 of common pharyngeal species per ml of the aspirate was found in 22 patients (class 3). The incidence of present or previous abnormalities of the common bile duct (choledocholithiasis, stenosis and dilatation) was 56% in class 1, and 13 and 20% in classes 2 and 3, resp. The mean age in classes 1, 2 and 3 was 68.2, 48.3 and 59.1 yr, resp. On the basis of a previous study it was anticipated that most of the patients in class 1, a considerable part of those in class 3 but almost none of those in class 2 harboured microorganisms in the liver and/or the biliary tract. As reflected by laboratory tests and the histology of the liver biopsy specimens, the incidence of liver disease appeared to be unrelated to the type of microflora in the upper small intestine. The incidence of an erythrocyte sedimentation rate above 30 mm/hour, urinary tract infection and concomitant diseases appeared to be higher in class 1 than in class 2. These findings indicate a possible relation between the duodenal microflora and the existence of an infectious process.

7202 INTESTINAL GANGRENE AS THE RESULT OF MESENTERIC ARTERIAL STEAL. *(E.)*

Connolly, J. E.; Stemmer, E. A. (Dept. Surg., Univ. California, Irvine). *Am. J. Surg.* 126(2):197-204, 1973.

Case reports are presented for 5 men, aged 44-69 yr, who developed intestinal ischemia and gangrene after arterial reconstruction for aortoiliac occlusive disease (aortoiliac steal syndrome). All 5 died. In all five patients there was unrecognized preoperative evidence of severe impairment of the mesenteric circulation. The significance of an enlarged central anastomotic artery on the preoperative aortogram was not appreciated and lateral views of the abdominal aorta were not obtained. A lateral aortogram would have shown the severe compromise of the origins of the celiac and superior mesenteric arteries in these patients. Shunting of blood into previously blocked leg vessels steals blood from the mesenteric circulation in a borrowing-lending fashion and can be critical to the viability of the bowel if the mesenteric circulation is already compromised. The mesenteric circulation must be severely compromised before aortoiliac reconstructive surgery in order for the steal to be significant. Therefore gangrene of the bowel after such surgery is not common. Patients having relatively fixed cardiac outputs are more likely candidates for aortoiliac steal, for increased distal flow cannot be compensated for by increased cardiac output. Such patients should be recognized prior to surgery and revascularization of the mesenteric circulation should be performed concomitantly with aortoiliac reconstruction.

7203 WHIPPLE'S DISEASE. EVOLUTION OF ULTRASTRUCTURAL LESIONS IN THE INTESTINAL MUCOSA DURING ANTIBIOTIC THERAPY: EIGHT CASES. *(Fr.)*

Marche, C.; Metayer, J.; Laumonier, R. (Bichat Hosp., Paris, France). *Ann. Anat. Pathol. (Paris)* 18(3): 309-327, 1973.

Biopsies of intestinal mucosa were taken at the level of the angle of Treitz from 8 men, aged 32-69 yr, before and during treatment with ampicillin (2 g/day) in 7 cases or hexacycline (1 g/day) in 1 case. Follow-up examinations were performed on 2 patients. Before treatment partial villous atrophy was present in 5 cases and absent in 3. The villi were club-shaped because of the presence of characteristic, periodic acid-Schiff (PAS) positive histiocytes in the lamina propria. Bacterial multiplication inside and outside of the histiocytes was observed in all cases, and lymphangiectasia and interstitial lacunae were present in 6 of the 8 patients. In contrast to classical findings, epithelial damage was present in all cases, and corn oil was absorbed slowly and unevenly by the intestinal epithelium in the 2 patients studied. During treatment epithelial repair paralleled the disappearance of extracellular bacteria, but the number of histiocytes decreased much more slowly. After 18-24 months of antibiotic therapy PAS-positive histiocytes, interstitial lacunae, and moderate collagen fibrosis were still present. Regeneration of microvilli and the disapperance of free bacteria in the lamina propria and basal epithelim occurred during the first week of treatment. After discontinuation of antibiotics, vacuolated macrophages and interstitial lacunae persisted, but no more bacteria were found and epithelial absorption was normal. These findings indicate that the epithelial changes are responsible for malabsorption in Whipple's disease. Interstitial lacunae may result from lipid stagnation or the excretion of bacterial degradation products by macrophages.

7204 A STUDY OF THE AETIOLOGY OF CONGENITAL STENOSIS OF THE GUT. *(E.)*

Earlam, R. J. (London Hosp., England). *Ann. R. Coll. Surg. Engl.* 51(2):126-128, 1973.

Congenital stenosis of the small bowel of the chicken embryo was produced by interrupting the blood vessels to the gut as contained in the umbilical hernia between the 9th and 17th days of development. From a total of 106 technically successful attempts to open the eggs, the loop of the bowel was lifted out in about 53 embryos and the mesenteric vessels were disrupted in 38. The remainder served as controls. Of the 20 embryos surviving, 15 were controls and 5 had the vessels divided longer than 24 hr. The major cause of death was presumably loss of blood either when the membranes were opened or when the mesenteric vessels were torn. Stenosis was seen in 3 of the 5 embryos in association with a defect in the mesentery where the vessels had originally been disrupted. The degree of stenosis was sufficient to cause proximal dilatation. No lesions occurred in control embryos. It is concluded that congenital stenosis of the small bowel may be caused by ischemia due to interruption of the arterial blood supply to gut caught in an umbilical hernia.

7205 NEW CONSIDERATIONS IN USE OF JEJUNOILEAL BY-PASS IN PATIENTS WITH MORBID OBESITY. *(E.)* Scott, Jr., H. W.; Dean, R.; Shull, H. J.; Abram, H. S.; Webb, W.; Younger, R. K.; Brill, A. B. (Vanderbilt Univ. Med. Ctr., Nashville, Tenn.). *Ann. Surg.* 177(6):723-735, 1973.

In 10 patients (group 1) the jejunum was divided 12 inches from the ligament of Treitz and anastomosed by its proximal end to the distal end of transected ileum 12 inches proximal to the ileocecal valve. In 21 patients (group 2) 12 inches of proximal jejunum was joined to the ileum 6 inches proximal to the ileocecal valve. Dietary restrictions and diphenoxylate hydrochloride (5 mg, 3-4 times/day) or codeine (15-30 mg, 3-4 times/day) were used to control early postoperative diarrhea. The only death occurred in a 486 pound male with a malignant carcinoid tumor of the midileum and metastases to mesenteric lymph nodes. Hepatitis developed in 2 cases, probably due to fluothane anesthesia. In group 1, maximal weight loss occurred in the first 12 months and leveled off around the 200 lb mark. The rate of weight loss was more rapid in group 2 with 8 patients falling below the 200 pound mark after 6 to 12 months; after 12 to 18 months several had reached their ideal weight. In group 2, diarrhea persisted for a slightly longer period, and greater malabsorption of d-xylose occurred. Serum vitamin C levels were consistently normal in group 1, but they tended to be somewhat diminished in group 2. In group 1 no supplementation was required to maintain normal serum calcium, magnesium and potassium levels. In 3 patients in group 2 prolonged supplementation with oral cations was required. In group 2, hypoalbuminemia was present in 8 of 14 patients in whom long range studies were made. In group 1 serum alkaline phosphatase and bilirubin were abnormal in only 2 patients. SGOT was elevated in 4 prior to and in 2 others following surgery; these levels tended to normalize quickly in all of these patients. In group 2, only the 2 hepatitis cases had elevated serum bilirubin, alkaline phosphatase, and SGOT values. Thus, ideal weight status is more likely to be achieved with the procedure used in group 2. However, the complications and side effects which accompany this procedure may be too severe for some patients. Therefore, this procedure has been restricted to patients weighing more than 350 pounds.

7206 SUPERIORITY OF ANTIPERISTALTIC JEJUNAL SEGMENTS IN MANAGEMENT OF SEVERE DUMPING SYNDROME. *(E.)* Sawyers, J. L.; Herrington, Jr., J. L. (Dept. Surg., Vanderbilt Univ., Nashville, Tenn.). *Ann. Surg.* 178(3):311-321, 1973.

A comparison is made of the effectiveness of 3 remedial operations for management of early postprandial dumping syndrome. Ten patients (5 males and 5 females, aged 39-60 yr) with isoperistaltic jejunal segments interposed between the gastric remnant and duodenum had no excellent results and good results were obtained in only 2 cases. In 12 patients (11 males and 1 female, aged 24-59 yr) with double iso-antiperistaltic jejunal limb pouch, excellent or good results were obtained in 7 (58%). Unfortunately, these pouches tend to dilate and empty poorly after several years. The best results were obtained by using a 10 cm single antiperistaltic jejunal segment interposed between the gastric remnant and duodenum in 28 patients (20 males and 8 females, aged 26-62 yr); 26 (93%) had good to excellent results. Follow-up studies extending to 11 yr demonstrate that these antiperistaltic segments continue to function effectively.

7207 MEDITERRANEAN LYMPHOMA WITH ALPHA-CHAIN DISEASE: BIOPSY AND AUTOPSY STUDY OF THE FIRST TUNISIAN CASE. *(Fr.)* Chadli, A.; Hafsia, M.; Maamouri, M. T.; Haddad, N.; Ayed, K. (Pasteur Inst., Tunis, Tunisia). *Arch. Anat. Pathol. (Paris)* 21(3):199-210, 1973.

A 17-yr-old male who came from southern Tunisia developed persistent diarrhea which failed to respond to symptomatic treatment, paroxysmal abdominal pain, and malnutrition with low blood calcium and sodium levels. A paraumbilical mass was observed on palpation, and radiological examination of the small intestine showed stenosis and compression. A diagnosis of α-chain disease was confirmed by immunoelectrophoresis and by histological examination of biopsies taken from the jejunum and an abdominal lymph node. Despite treatment with a combination of antibiotics, corticosteroids, vincristine, and procarbazine, the patient died 2.5 yr after onset of symptoms. Autopsy showed involvement of the prepancreatic, retroperitoneal, and pericecal lymph nodes and, to a lesser extent, the mediastinal and cervical lymph nodes and right tonsil. No infiltrates were found in the spleen, bone marrow, or liver, confirming that α-chain disease affects primarily the small intestine and abdominal lymph nodes.

7208 CARCINOID TUMOR OF THE SMALL INTESTINE WITH HEPATIC METASTASES CONTAINING LARGE

AMOUNTS OF THYROCALCITONIN ASSOCIATED WITH A BENIGN C-CELL ADENOMA OF THE THYROID. *(Fr.)* Cattan, D.; Pappo, E.; Dervichian, M.; Melliere, D.; Chelloul, Y.; Calmettes, C.; Milhaud, G. (St. Antoine Fac. Med., Paris, France). *Arch. Fr. Mal. Appar. Dig.* 62(2):141-150, 1973.

A 47-yr-old woman who had developed a goiter during adolescence and had a 2-yr history of diarrhea was hospitalized with hepatomegaly. The blood thyrocalcitonin (TCT) level was increased to 5.5 ng/ml (radioimmunological technique), as were plasma serotonin (0.96 and 0.99 µg/ml) and urinary excretion of 5-hydroxyindolylacetic acid (5-HIAA; 90 mg/24 hr). At laparotomy a carcinoid tumor was found in the jejunum with multiple hepatic metastases, and a benign C-cell adenoma was present in the thyroid. TCT was found in the jejunal carcinoid (1.7 ng/mg), hepatic metastases (62.2 ng/mg), and thyroid adenoma (5.5 ng/mg). The short-term results of surgery (resection of the jejunal carcinoid and total thyroidectomy) were good, but diarrhea persisted and gradually became incapacitating, and a malar flush became more pronounced. Three months after surgery, plasma serotonin had risen to 1.82 µg/ml and urinary 5-HIAA excretion had increased to 284.1 mg/24 hr. Tests for blood TCT were negative 4 and 7 months after surgery. Intestinal obstruction and collapse developed suddenly 10 months after surgery, and the patient died after resection of an infarct in the small intestine. The level of blood TCT found before surgery was compatible with diagnosis of a medullary thyroid carcinoma, but the levels of plasma serotonin and urinary 5-HIAA excretion were significantly greater than those produced by carcinomas of the thyroid medulla. It is difficult to account for the absence of TCT found after surgery despite the very high levels of TCT present in hepatic metastases of the carcinoid. Perhaps carcinoids secrete TCT intermittently.

7209 THE OBSTRUCTIVE FORM OF GASTROINTESTINAL AMYLOIDOSIS AS A MANIFESTATION OF A MYELOMA: PRESENTATION OF ONE CASE. *(Fr.)* Geffroy, Y.; Colin, R.; Duprey, F.; Hemet, J.; Tayot, J.; Hecketsweiler, P.; Galmiche, J. P. (Charles Nicolle Hosp., Rouen, France). *Arch. Fr. Mal. App. Dig.* 62(5):399-409, 1973.

Radiological examination of a 71-yr-old man, hospitalized for vomiting bile several times a day, showed pronounced distension of the small intestine and failure of barium to pass beyond the 3rd loop of the small intestine. At laparotomy almost the entire small intestine appeared to be grey, thickened, granite-like, and fleshy. A biopsy of the small intestine revealed the presence of amyloid deposits. Serum IgG and IgM levels were decreased and the IgA level was increased. The presence of a λ and κ type globulin was established by using antisera for light chain globulins. The diagnosis of myeloma was confirmed by a bone marrow biopsy in which 42% of the cells were tumor plasma cells. No radiological evidence of a bone anomaly was found. Intestinal obstruction did not respond to prostigmine, passage of a rectal tube, or aspiration of the gastric contents. The patient died with pneumococcal septicemia 1.5 months after the onset of symptoms. Autopsy showed pronounced gastrointestinal amyloidosis which involved the antropyloric region, small intestine and, to a lesser extent, the colon. No abnormal plasma cell infiltration was present in the gastrointestinal tract.

7210 MORPHOLOGICAL STUDY OF EXPERIMENTAL REVASCULARIZATION OF THE ISCHEMIC INTESTINE. *(Fr.)* Winninger, A. L.; Sudan, N.; Leenhardt, P.; Monticelli, J.; Lebreuil, G.; Devin, R. (St. Marguerite Hosp., Marseille, France). *Arch. Fr. Mal. App. Dig.* 62(4):315-321, 1973.

Acute ischemia of the small intestine was induced in 29 dogs by clamping off the superior mesenteric artery and vein for 4 hr and ligating the intestine and its arcade from the duodenum to the terminal part of the colon. Three precautions were taken to avoid high mortality: (1) isolation of the autonomic nervous system in the intestine by injection of alcohol and resection of the mesenteric plexus around the origin of the superior mesenteric artery; (2) maintenance of satisfactory arterial pressure; and (3) diversion of intestinal lymph by draining the thoracic canal. During ischemia lesions in the small intestine were limited to the mucosa; muscle fibers showed no signs of degeneration. Desquamation and capillary dilatation were observed on the villi, and thrombi of fibrin and platelets formed after 3 hr. Liver changes were minimal. During revascularization changes included subtotal epithelial necrosis with rupture of some capillaries in the villi; glandular crypts remained almost intact. Degenerative changes were observed in the muscle fibers (microvacuoles, loss of color). Venous thrombi which had developed during ischemia disappeared. Large extrahepatic blood clots containing RBC were found in 25 of 29 dogs, and microthrombi were present in the portal venules in 28. Liver damage occurred in only 3 cases and consisted of centrilobular necrosis, periportal necrosis, and an infarct, resp. These findings do not rule out the possibility that intestinal changes induced by ischemia are reversible.

7211 CONGENITAL SHORT BOWEL. *(E.)* Kern, I. B.; Harris, M. J. (Prince Wales Hosp., Randwick, Australia). *Aust. N.Z. J. Surg.* 42(3):283-285, 1973.

A case report is presented for a 7-week-old boy with short bowel syndrome and no exteriorization of the small intestine. The patient presented with symptoms suggestive of a chronic partial intestinal obstruction. X-ray examination showed a grossly dilated small intestine and malrotation. At laparotomy the small intestine measured 70 cm from pylorus to ileocecal value (normal length 220-250 cm), and hypertrophic pyloric stenosis was also present. A pyloromyotomy and a Ladd-Bill procedure were performed, but ileus persisted so that a second laparotomy was performed 2 weeks after the first to determine whether a partial block was present in the terminal ileum. Adhesions were found, but these would probably not have impeded normal bowel function. During continuous duodenal deflation by aspiration it was found that the duodenal aspirate and fecal discharge were strongly acid. Administration of bicarbonate p.o. stimulated propulsion along the small intestine, but peristalsis did not reach the final segment of the small intestine. Attempts to introduce oral finding with glucose water and Vivonex 100 only increased the duodenal aspirate and increased fecal discharge. Jejunal and rectal biopsies were normal. After discontinuation of i.v. feeding the patient died at age 20 weeks. Since all 3 reported cases of congenital short bowel have also displayed malrotation, there may be a relation between these two anomalies. It is postulated that vascular insufficiency may occur at a crucial time during development of the small intestine, when it is still in the extraembryonic coelom. Instead of causing a localized infarct, this insufficiency results in atresia and halts a normal period of rapid growth. The failure of the small intestine to elongate at this time might be the cause of the malrotation, rather than its effect. Ischemia of the intestine might also leave it dilated and semiparalyzed.

7212 INTRAMURAL HAEMORRHAGE OF THE BOWEL COMPLICATING ANTICOAGULANT THERAPY. *(E.)*

Sheiner, H. J.; Glancy, J. J. (Sir Charles Gairdner Hosp., Perth, Australia). *Aust. N.Z. J. Surg.* 42(4):341-345, 1973.

The occurrence of intramural hemorrhage in 4 patients (3 males and 1 female, aged 61-88 yr) receiving anticoagulant therapy for periods of 1-8 months is reported. Presenting symptoms may easily be confused with intestinal obstruction. The use of barium studies is encouraged as an aid in diagnosis. Abnormal bleeding from other sites was evident in 3 of these 4 patients as hematuria and in 2 as skin bruising. Poor control of anticoagulant therapy existed in 3 cases. Prothrombin time was within the therapeutic range in 1 case. All 4 were treated conservatively, with i.v. fluids, nasogastric suction, and correction of prothrombin times. Recovery was complete within 3 weeks. Surgery as a routine measure in these cases is not recommended.

7213 USE OF ELEMENTAL DIET DURING THE ADAPTIVE STAGE OF SHORT GUT SYNDROME. *(E.)*

Voitk, A. J.; Echave, V.; Brown, R. A.; Gurd, F. N. (McGill Univ. Surg. Clin., Montreal, Canada). *Gastroenterology* 65(3):419-426, 1973.

An elemental diet was used during the adaptive phase of the short gut syndrome in 8 patients. The length of small bowel, measured from the ligament of Treitz, ranged from 50-200 cm. Hemicolectomy had been performed in 3 patients; total colectomy in 2. The etiology was determined to be radiation enteritis (1), repeated resections for complications from regional enteritis (4), massive resection after superior mesenteric artery thrombosis (1), metastatic leiomyosarcoma (1), and Gardner's syndrome with a desmoid tumor (1). Of the 8 patients, a fistula was present in 4. The diet, delivered by nasogastric catheter, was well tolerated and positive nitrogen balance was achieved. The average weight gain was 3.3 kg/month for the group. Adaptation in 4 patients was sufficient to tolerate normal food. One patient underwent major surgery which he withstood well, and eventually had intestinal continuity restored. There were 3 deaths, 2 from their disease and 1 from aspiration. The latter case demonstrates the importance of radiographic verification of nasograstric tube position prior to diet infusion. Provided that care is taken with tube position, no serious complications with this technique are encountered. Elemental diet is a useful addition to the nutritional armamentarium in the treatment of short gut syndrome, if sufficient absorptive surface is left. In extremely short bowels, even a predigested elemental diet may not be absorbable initially, but adaptation may provide sufficient absorptive surface to allow eventual chronic use of elemental diet in preference to permanent i.v. hyperalimentation.

7214 INTESTINAL SHUNT-OPERATION IN OBESITY. A COMPARISON OF THREE TYPES OF OPERATION.

(E.) Dano, P.; Jarnum, S.; Nielsen, O. V. (Rigshospital, Copenhagen, Denmark). *Scand. J. Gastroenterol.* 8(5):457-464, 1973.

Jejunoileal anastomosis proved effective in the treatment of 36 obsese patients (12 males and 24 females), aged 15-58 yr). In most cases side effects were so minimal that the operation is recommended for selected cases of severe obesity. The indication for surgery was morbid obesity in 31 cases and adiposogenital dystrophy in the other 5. Abnormalities in liver function tests were not pronounced, and severe disturbances in plasma electrolytes occurred in only 2 cases. Three types of operations were compared: end-to-side anastomosis between jejunum 36 cm from the ligament of Treitz and ileum 12 cm from the cecum (type I), between 24 cm of jejunum and 24 cm of ileum (type II), and between 12 cm jejunum and 36 cm ileum (type III). The type of operation performed had no effect on the amount of weight lost. Side effects were also of the same frequency in the 3 groups. Absorption of vitamin B_{12} was much better in type III patients with a long ileal segment than in type I patients with a short ileal segment. One patient died of pulmonary embolism and cerebral thrombosis 11 months after surgery. Of these 3 types of operation, type III is recommended.

7215 EXPERIMENTAL INTESTINAL ISCHEMIA: PROVOCATIVE ABSORPTION STUDIES FOLLOWING GRADUAL CELIAC AND SUPERIOR MESENTERIC ARTERY OCCLUSION. *(E.)*

Stanley, J. C.; Brink, B. E.; Fry, W.

J. (Univ. Michigan, Med. Ctr., Ann Arbor). *J. Surg. Res.* 14(2):133-138, 1973.

Intestinal absorption of d-xylose was studied in 10 adult dogs with celiac artery occlusion, 5 with superior mesenteric artery occlusion, and 5 with both celiac and superior mesenteric artery occlusion. There was no significant change in d-xylose absorption following provocative feedings of meat in control animals. Thus, provocative meals do not influence d-xylose absorption when there is intact splanchnic circulation. Celiac artery occlusion did not affect d-xylose absorption when no meal was given previously. Therefore, d-xylose absorption tests cannot be used to document celiac artery obstruction. When tested during the postprandial period, however, impaired d-xylose absorption was evident; the mean differences at 2 and 5 hr postprandial were 20.9 and 6.0 mg/100 ml, resp. Superior mesenteric artery occlusion caused no significant change in absorption whether with or without provocative feedings. Coexisting celiac and superior mesenteric artery occlusion caused no significant differences in absorption of d-xylose administered alone. Provocative feedings after celiac and superior mesenteric artery occlusion decreased absorption by 35.2 and 10.2 mg/100 ml at 2 and 5 hr, resp. Impairment of d-xylose absorption by celiac artery occlusion was attributed to the effect of collateral circulation on blood flow velocity within the superior mesenteric artery and altered perfusion of its distal branches.

7216 PERFORATION IN ACQUIRED DIVERTICULAR DISEASE OF THE TERMINAL ILEUM. *(E.)* Crowley, J. G. (Univ. Maryland Hosp., Baltimore). *m. Surg.* 39(9):514-517, 1973.

7217 VILLOUS TUMOUR OF THE DUODENUM. REPORT OF A CASE AND REVIEW OF THE LITERATURE. *(E.)* arbier, J.; Breuil, J.; Blavon Duchesne, N.; Babin, .; Beauchant, J. (Hosp. Ctr., Univ. Poitiers, rance). *Arch. Fr. Mal. App. Dig.* 62(4):323-329, 973.

218 CHANGES IN THE MUCOSA OF THE SMALL INTESTINE IN ACUTE DYSENTERY. (CLINICAL AND ORPHOLOGICAL STUDY). *(Rus.)* Bliuger, A. F.; inel'nikova, M. P.; Veksler, Kh. M.; Terent'eva, . A.; Novitskii, I. N. (Riga Med. Inst., USSR). *rkh. Patol.* 35(2):38-43, 1973.

219 DUPLICATION OF THE SMALL BOWEL WITH PEPTIC ULCER PERFORATION. *(E.)* Niesche, J. W. Sydney Hosp., Australia). *Aust. N.Z. J. Surg.* 2(4):356-358, 1973.

220 HISTOLOGICAL FOLLOW-UP OF DUODENITIS. *(E.)* Cheli, R.; Aste, H.; Ciancamerla, . (San Martino Hosp., Genoa, Italy). *Endoscopy* (3):135-139, 1973.

7221 MECKEL'S DIVERTICULUM AND ITS COMPLICATIONS IN CHILDREN. *(Ger.)* Morger, R. (Eastern Switzerland Hosp. Infants and Children, St. Gallen). *Helv. Chir. Acta* 39(5/6):797-799, 1972.

7222 MESENTERIC ARTERITIS WITH EXTENSIVE INTESTINAL GANGRENE. *(E.)* Nygaard, K.; Flatmark, A. (Rikshosp., Oslo, Norway). *Acta Chir. Scand.* 139(5):470-475, 1973.

7223 CHRONIC IDIOPATHIC INTESTINAL PSEUDO OBSTRUCTION. *(Sp.)* Bercetche, M.; Kravetz, D.; Cantor, D. (A. Posadas Polyclin., Haedo, Argentina). *Acta Gastroenterol. Latino Am.* 4(4):161-165, 1972.

7224 JAUNDICE AND PANCREATITIS CAUSED BY A DUODENAL DIVERTICULUM. *(E.)* Wilk, P. J.; Mollura, J.; Danese, C. A. (Mt. Sinai Hosp., New York, N.Y.). *Am. J. Gastroenterol.* 60(3):273-279, 1973.

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7306 INTRAMURAL HEMATOMA OF THE SMALL INTESTINE IN THE COURSE OF ANTI-COAGULANT THERAPY. *(Fr.)* Gautier-Benoit, C.; Houcke, M.; Pinchon, J. (Lens Hosp. Ctr., France). *Lille Med.* 17(7):998-1000, 1972.

See also, 6713, 6727, 6750, 6771, 6787, 6795, 6810, 6814, 6826, 6828, 6844, 6854, 6866, 6872, 6879, 6893, 6913, 7013, 7025, 7059, 7104, 7123, 7159, 7310, 7399, 7465, 7532, 7549, 7578, 7913, 7981, 7993, 8030, 8088, 8092, 8093, 8095, 8166, 8203, 8225.

SMALL INTESTINE

Malabsorption

307 THE DISTRIBUTION AND DEGRADATION OF ALBUMIN
IN TROPICAL SPRUE: I. A COMPARATIVE ANA-
YSIS OF ALBUMIN TURNOVER DATA USING DIFFERENT
ATHEMATICAL MODELS. *(E.)* Singh, B.; Jeejeebhoy,
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lbumin turnover studies with ^{131}I-labeled human
erum albumin were conducted on 11 controls and 28
atients with tropical sprue. The turnover data were analyzed by various mathematical models and by analogue computer. These studies showed that the fractional catabolic rate can be in error when only intravascular radioactivity data are analyzed. Values for extravascular albumin obtained by computer analysis are distinctly higher than values obtained by other methods but are closer to the estimate made recently by immunochemical analysis of samples from various extravascular sites of albumin. All of the mathematical models used gave similar values for the albumin pool in patients with

tropical sprue and controls. Because of hypoalbuminemia there was a concomitant decrease in intravascular and extravascular albumin in tropical sprue. The fractional catabolic rate and the ratio of extravascular to intravascular albumin levels were also comparable to control values. Thus, the hypoalbuminemia which occurs in tropical sprue can be accounted for by reduced albumin synthesis.

7308 PROTEIN-LOSING ENTEROPATHY IN CHILDREN. *(E.)* Colon, A. R.; Sandberg, D. H. (Univ. Miami Sch. Med., Fla.). *South. Med. J.* 66(6):641-644, 1973.

A review has been made of 15 children (8 boys and 7 girls, aged 1 month to 9 yr) with protein-losing enteropathy caused by milk allergy (3), parasitic disease (2), celiac disease (2), Menetrier's disease (1), Crohn's disease (1), and unknown causes (6). Diarrhea, edema and ascites were the most common presenting complaints, occurring in 50% of these cases. Heights and weights of 8 of these children were below the 3rd percentile. Following therapy, 5 of these 8 have reached the 10th-25th growth percentile. None of these patients received therapeutic iron, but 2 required initial transfusions of whole blood. Symptoms in cases of milk allergy abated with cessation of milk ingestion. Edema and diarrhea cleared in the 2 with parasitic disease within 8 days after antihelminthics effective against *Ascaris* and *Trichuris trichura* were instituted. Idiopathic protein-losing enteropathy resolved spontaneously in 3 children. It is suggested that when protein loss is shown by radiolabeled macromolecules, examination of the bowel for underlying lesions is in order. It is concluded that identification of the etiology of protein-losing enteropathy and treatment of the underlying disorder improve growth in these children.

7309 ALPHA-CHAIN DISEASE IN SUBSAHARAN AFRICA. *(E.)* Novis, B. H.; Kahn, L. B.; Bank, S. (Groote Schuur Hosp., Cape Town, South Africa). *Am. J. Dig. Dis.* 18(8):679-688, 1973.

The first 2 cases of α-chain disease in sub-Saharan Africa are reported in 2 young mulatto patients (a 29-yr-old male and a 16-yr-old female) with malabsorption, a prominent plasma cell infiltrate of the lamina propria of the small bowel, and abdominal lymphoma. The reticulum cell lymphoma involved mesenteric nodes in both patients and the small bowel in one of them. Abnormal α-chain disease protein was demonstrated in their sera; this disappeared after radiotherapy (3000 rads cobalt to the central abdomen over about 45 days) and steroid therapy (40-60 mg/day initially) induced a clinical remission. The dramatic response of 1 patient to cortisone suggests that malabsorption resulted from the plasma cell infiltrate and villous atrophy rather than from the malignant lymphoma.

7310 ULCERATION OF THE SMALL INTESTINE COMPLICATING CELIAC DISEASE. *(E.)* Seliger, G.; Goldman, A. B.; Firooznia, H.; Lawrence, L. R. (New York Univ. Sch. Med., New York). *Am. J. Dig. Dis.* 18(9):820-824, 1973.

A 60 yr old male was admitted with a 20 yr history of intermittent diarrhea, low abdominal cramps, and rectal flatus. Laboratory studies showed SGOT, 24 U; alkaline phosphatase, 6.2 U; bilirubin, 0.4 mg/100 ml; and blood urea nitrogen, 23 mg/100 ml. Nontropical sprue was diagnosed. A gluten-free diet controlled the symptoms until an exacerbation occurred. Anorexia and weakness accompanied the severe abdominal cramps and diarrhea. A 10 lb weight loss was noted. There had been a 30 yr history of moderate alcohol consumption. Examination of the upper gastrointestinal tract and small bowel revealed a smooth eccentric area of stenosis of the second portion of the duodenum with an ulcer crater on the medial wall. Moderate dilatation of the small intestine with loss of the normal feathery appearance of the mucosal folds in the jejunum was observed. Small bowel biopsy revealed clubbing and atrophy of villi. A gluten-free diet relieved the pain, but weight loss continued. Pitting ankle edema, probably due to hypoalbuminemia, developed. In cases of ulceration complicating sprue, surgical resection of the ulcer is suggested as the only effective treatment.

7311 PLASMA FOOD ANTIBODIES DURING WITHDRAWAL AND REINTRODUCTION OF DIETARY GLUTEN IN COELIAC DISEASE. *(E.)* Carswell, F.; Ferguson, A. (Roy. Hosp. Sick Children, Bristol, England) *Arch. Dis. Child.* 48(8):583-586, 1973.

Of 55 children with celiac disease, 40 had food antibodies in their plasma at diagnosis. After 2 months on a gluten-free diet, the antibodies disappeared in all but 6 of 21 patients. Of these 6 patients 5 had high plasma IgA levels at diagnosis. Reintroduction of wheat and rye gluten was accompanied by intermittent presence of plasma food antibodies in 7 of 8 patients subsequently shown to have the small bowel biopsy appearances of celiac disease. In 4 patients whose biopsies were normal after reintroduction of gluten, plasma food antibodies did not appear. A single test for plasma food antibodies did not reliably indicate minor deviations from the gluten-free diet in established celiac patients.

7312 PLASMA β_1C-β_1A GLOBULINS AND IMMUNOGLOBULINS IN COELIAC DISEASE. *(E.)* Carswell, F.; Logan, R. W. (Roy. Hosp. Sick Child., Glasgow, Scotland). *Arch. Dis. Child.* 48(8):587-589, 1973.

Immunoglobulin and β_1C-β_1A globulin concentrations were estimated in 35 children with untreated celiac disease and in 33 other children by a Mancini technique. Of the 33 controls, probable gastrointestinal disease was present in 22 of them including diagnoses of *Giardia lambia* infestation (11), psychosocial diarrhea (8), post-gastroenteritis syndrome (2), cystic fibrosis (2), Milroy's disease with gut involvement (1), sex-linked a-γ-globulinemia (1), low birthweight dwarfism (1), constitutional dwarfism

(1), hypothalmic astrocytoma (1), familial hypophosphatemic rickets (1), and iron deficiency malabsorption (1). The mean β_1C-β_1A concentration was reduced to 108 mg/100 ml in the celiac group *vs.* 121 mg/100 ml in controls, due either to reduced production or increased consumption. Mean IgA level was 131 mg/100 ml in celiac patients *vs.* 98 mg/100 ml in controls. No significant differences occurred in the IgG and IgM concentrations. The low β_1C-β_1A globulin concentration in celiac disease patients is consistent with the theory that celiac disease is due to an Arthus-type reaction in the lamina propria between immunoglobulins, antigens, and complement. The complex which results is thought to damage the enterocytes. No correlation was evident between infection and low complement levels.

7313 THE INCREASED RATE OF LOSS, AND NON-EXPONENTIAL EXCRETION OF BILE SALTS IN PATIENTS WITH TROPICAL SPRUE AND ILEECTOMY. *(E.)* Kapadia, C. R.; Baker, S. J. (Christian Med. Coll. Hosp., Vellore, India). *Aus. N.Z. J. Med.* 3(3):260-263, 1973.

^{14}C-Carboxyl-labeled cholic acid (5 or 10 µCi) was infused i.v. into 5 controls with no evidence of malabsorption, 7 patients with tropical sprue, and 2 patients with ileal resection. The daily fecal excretion of radioactive material was measured for 7-13 days. Patients with tropical sprue all had steatorrhea, xylose malabsorption, and barium meal and jejunal biopsy changes; 5 also had vitamin B_{12} malabsorption. Patients with ileal resection had steatorrhea and vitamin B_{12} malabsorption. In contrast to other reports in the literature, 2 patients with ileal resection, 4 with tropical sprue, and 1 control had decay curves which were not exponential; this was most evident in patients with the greatest initial excretion of radioactive material. This indicates that it is not valid to calculate rate constants from fecal excretion studies. The rate of excretion was increased in 4 of the 7 patients with sprue; in 2 cases the decay curves were in the range of the 2 patients with ileal resection, indicating that reabsorption of bile salts is impaired and that excessive bile salt loss may be important in the pathogenesis of some cases of tropical sprue. No direct correlation was observed since other factors, such as impairment of fatty acid absorption caused by cell damage in the jejunal mucosa, are also important in the pathogenesis of tropical sprue.

7314 PROTEIN-LOSING ENTEROPATHY IN DERMATITIS HERPETIFORMIS. *(E.)* Toft, A. D.; Heading, R. C.; Simpson, J. (Roy. Infirm., Edinburgh, Scotland). *Br. J. Dermatol.* 89(3):233-236, 1973.

A 57-yr-old male coal miner presented with generalized edema. His history included 15 years of dermatitis herpetiformis. Urinary protein excretion was consistently below 2.0 g/day. The patient experienced spontaneous recovery, but was readmitted with generalized edema 6 months later. Jejunal biopsy revealed subtotal villous atrophy. The patient was treated with a gluten-free diet to reverse protein loss. The patchy nature of the lesion preculuded a valid biopsy assessment of response to this treatment. Gross intestinal protein loss occurred in association with an otherwise typical dermatitis herpetiformis enteropathy and no other gastrointestinal abnormality. An episode of glomerulonephritis may have contributed to the initial edema, but it could not account for persistent hypoproteinemia. It is noted that in this case, as well as in 2 previously reported cases of protein-losing enteropathy in dermatitis herpetiformis, the serum cholesterol level was significantly elevated in contrast to subnormal levels of cholesterol found in celiac disease.

7315 MUCOSAL ULCERATION AND MESENTERIC LYMPHADENOPATHY IN COELIAC DISEASE. *(E.)* Jones, P. E.; Gleeson, M. H. (Whittington Hosp., London, England). *Br. Med. J.* 3(5873)212-213, 1973.

A 58-yr-old male was hospitalized with upper abdominal distension of 4 months duration plus frequent pale loose stools (up to 8/day). Liver function tests revealed serum bilirubin, 0.7 mg/100 ml; alkaline phosphatase 38/King-Armstrong U. units; BSP retention, 40% at 45 min; IgA, 740 mg/100 ml; and IgM, 150 mg/100 ml. laparotomy was carried out for possible lymphoma. The distal jejunum showed thickening of the bowel wall in 3 segments, with dilated bowel proximal to these segments. Enlarged, firm lymph nodes were present throughout the small bowel mesentery. Patchy ulceration with plasma cell and polymorphonuclear infiltration and fibrosis extended through the muscularis. Perilobular fatty infiltration was present in the liver. After 3 weeks of gluten withdrawal with no clinical improvement, prednisolone (60 mg/day) was administered. Anticoagulation therapy with heparin (i.v.) followed by phenindione (p.o.) was instituted following a right subclavian vein thrombosis and multiple pulmonary emboli. Seven weeks postoperatively, additional surgery was required to remove a constriction caused by a fibrous band at the site of the previous biopsy in the jejunum. The rest of the small intestine appeared normal: lymph nodes had decreased in size and mesenteric thickening was less marked, but partial villous atrophy and chronic infiltration by inflammatory cells were found in the proximal jejunum. Follow-up biopsies revealed the normal predominance of IgA and marked improvement, although partial villous atrophy persisted 8 months after the first operation. The etiology of small intestine ulceration in celiac disease is unknown. It is possible that abnormalities in immunoglobulins secreted into the intestinal lumen may allow food antigens to damage the mucosa and cause ulceration.

7316 GAS CHROMATOGRAPHIC ANALYSIS OF URINARY VOLATILE PHENOLS IN PATIENTS WITH GASTROINTESTINAL DISORDERS AND NORMALS. *(E.)* Duran, M.; Ketting, D.; De Bree, P. K.; van der Heiden, C.;

Wadman, S. K. (Wilhelmina Children's Hosp., Utrecht, Netherlands). *Clin. Chim. Acta* 45(4):341-347, 1973.

Urinary excretions of phenol and p-cresol were determined in 16 patients (aged 1 yr through adult) with ileal resection (2), celiac disease (8), enteritis (3), cystic fibrosis (2), and sub-total ileal resection (1). Diet was normal in protein content. Of these 16 patients, 15 had abnormal excretion of at least 1 of the following substances: urinary benzoic acid, phenylacetic acid, p-hydroxybenzoic acid, or p-hydroxyphenylacetic acid, thus indicating increased bacterial metabolism of tyrosine or phenylalanine. Of 20 analyzed samples, 9 had increased phenol and 14 had increased p-cresol, with the highest p-cresol excretions occurring in 4 celiac disease patients and the 1 sub-total ileal resection patient. The sum of phenol excretion does not exceed 0.01 mmole/g creatinine and unconjugated p-cresol, 0.03 mmole/g; both are very low compared to conjugated compounds. These results support the suggestion that phenol and p-cresol are produced by microflora in the colon from undigested protein and/or unabsorbed amino acids. It is concluded that phenol and p-cresol are important in bacterial tyrosine metabolism in gastrointestinal disease patients. It is also concluded that increased urinary p-cresol and phenol, especially combined with increased benzoic and phenylacetic acid, demand gastrointestinal investigation.

7317 INTESTINAL INVOLVEMENT IN WALDENSTROM'S MACROGLOBULINEMIA.

(E.) Bedine, M. S.; Yardley, J. H.; Elliott, H. L.; Banwell, J. G.; Hendrix, T. R. (Johns Hopkins Univ. Sch. Med., Baltimore, Md.). *Gastroenterology* 65(2):308-315, 1973.

A 68-yr-old woman with Waldenstrom's macroglobulinemia presented with malabsorption and weight loss. Deposits of hyaline material in the lamina propria of the small intestine produced bizarre, clubbed villi and were associated with large foamy macrophages of uncertain origin. There were also various lymphoid cells in the lamina propria that included plasma and plasmacytoid cells having amorphous intranuclear inclusions of the type often found in Waldenstrom's macroglobulinemia. The hyaline material deposited in the villi appeared to be macroglobulin. Local production of macroglobulin by abnormal lymphoid cells in the villi may contribute to its deposition there. The deposits were probably a major factor causing malabsorption.

7318 IMMUNOCHEMICAL STUDY OF THE MALABSORPTION SYNDROME WITH COW'S MILK INTOLERANCE.

(E.) Savilahti, E. (Children's Hosp., Helsinki, Finland). *Gut* 14(6):491-501, 1973.

The effect of cow's milk provocation on immunoglobulins in intestinal mucosa, intestinal juice, stool extracts, as well as on the levels of antibodies to cow's milk and β-1 C/A in serum, was studied in 18 infants, (8 males and 10 females) with the malabsorption syndrome. The infants improved on breast milk and were therefore suspected to be intolerant to cow's milk and challenged with it. At the time of clinical relapse a marked and uniform increase in the numbers of IgA- and IgM-containing cells, (2.4 times as many on the average as before challenge), was observed in the jejunal mucosa of 8 reacting patients at 9 provocations with cow's milk. There was no abnormality in the immunoglobulin-containing cells before challenge or in biopsy specimens taken shortly after the resumption of the elimination diet (breast milk). The clinical reaction was preceded 1-5 weeks by a pronounced rise in the IgA and IgM contents of stool extracts, and a rise in the titer of hemagglutinating antibodies and serum IgA, changes which subsided rapidly after withdrawal of cow's milk. IgE levels in these patients were low (50-150 IU/ml) and no rise took place during provocation. No fall in β-IC/A concentration occurred in serial samples. In some of the 10 patients who tolerated cow's milk challenge clinically, there was an increase in both IgA- and IgM-containing cells suggestive of a local immunological reaction although no clinical intolerance was provoked and other immunological signs were weak or absent. In other nonreacting patients, no immunological reaction was noted. Therefore, it is evident that cow's milk is the agent responsible for the strong local intestinal reaction coinciding with the clinical symptoms.

7319 NATURE OF TOXIC COMPONENT OF WHEAT GLUTEN IN COELIAC DISEASE.

(E.) Dissanayake, A. S.; Truelove, S. C.; Offord, R. E.; Whitehead, R. (Radcliffe Infirm., Oxford, England). *Lancet* (7831):709-710, 1973.

Ultrafiltration of a peptic/tryptic digest of gluten yielded 3 fractions, 2 of which were toxic to 3 patients with celiac disease controlled by a gluten-free diet. The harmless fraction consisted of electrolytes, amino acids, and oligopeptides. One of the toxic fractions contained polypeptides, a large portion of which had a molecular weight of about 8000, which is much lower than the 55,000 molecular weight of α-gliadin. Thus, gliadin does not appear to be the toxic component in gluten.

7320 LOSS OF PROTEIN FROM THE GASTROINTESTINAL TRACT IN WALDENSTROM'S MACROGLOBULINEMIA.

(Ger.) Diewitz, M. (Med. Polyclin., Univ. Cologne, Germany). *Munch. Med. Wochenschr.* 115(28):1285-1287, 1973.

The Gordon test with ^{51}Cr-labeled serum albumin showed that 2 of 4 patients with Waldenstrom's macroglobulinemia excreted abnormally large quantities of protein in their stools. Within the first 4 days after administration of 100 mCi of ^{51}Cr-labeled albumin, a 47-yr-old man excreted 16.9% and a 65-yr-old man, 1.12% of the dose administered.

ince other investigators have demonstrated that low
olecular weight proteins, rather than macroglobu-
ins, are excreted in the stools and since no macro-
lobulins have been found in the stomach, this pro-
ein-losing enteropathy is probably not caused by
astrointestinal involvement in Waldenstrom's macro-
lobulinemia. Instead, protein-losing enteropathy
ay be due to increased capillary permeability and
ragility. No correlation was found between pro-
ein-losing enteropathy and serum albumin or macro-
lobulin levels in these patients.

7321 INHERITANCE AND INFLUENCE OF HISTOCOMPATIBILITY (HL-A) ANTIGENS IN ADULT COELIAC
ISEASE. *(E.)* Stokes, P. L.; Asquith, P.; Holmes, G.
. T.; MacKintosh, P.; Cooke, W. T. (Gen. Hosp.,
irmingham, England). *Gut* 14(8):627-630, 1973.

istocompatibility (HL-A) antigen determinations were
arried out in 117 patients with adult celiac disease
nd 149 of their first-degree relatives, of whom 94
ad a jejunal biopsy performed. There was an increase
requency of the HL-A 8 and HL-A 1 antigens in celiac
atients (80.3 and 70.1%, resp.) compared with 268
ontrols (20.5 and 33.2%, resp.). The frequency of
ne combination of these 2 antigens was 65.8% in ce-
iac patients and only 20.1% in controls. Among 101
irst-degree relatives of 48 patients with HL-A 8,
ne approximate percentage distribution of the anti-
en was fathers, 87%; mothers, 60%; brothers, 73%;
isters, 87%; sons, 56%; and daughters, 50%. In 5 of
families in which both parents of an HL-A 8 celiac
atient were typed, both father and mother were HL-A
; the fathers were HL-A 8 in the other 3. In 6
amilies studied for inheritance of celiac disease,
parents who transmitted the HL-A 1 and 8 haplotype
their celiac children did not have the disease
nemselves, while 3 other parents who had similarly
assed on the haplotype did have the disease. Four
nildren inherited this haplotype from a celiac par-
nt but did not have celiac disease. The data indi-
ate that inheritance of HL-A antigens in celiac fam-
lies is straightforward and follows Mendelian prin-
ples. Inheritance of the HL-A 1 and 8 haplotype by
member of a celiac family need not be associated with
nheritance of the disease.

322 SERUM ANTI-RETICULIN ANTIBODY AS FURTHER EVIDENCE OF THE INCREASED IMMUNE RESPONSE
DIETARY ANTIGENS IN COELIAC CHILDREN. *(E.)*
overna, M.; Franchini, I.; Della Cella, G.; Durand,
. (Inst. Ind. Med., Univ. Genoa, Italy). *Helv.*
ediatr. Acta 28(3):267-273, 1973.

ntibody to reticulin was tested in the sera from
celiac children (11 males and 13 females, aged
months to 4 yr) by indirect immunofluorescence.
ome dietary antigens were also tested using passive
emagglutination. Sera from 11 celiac patients
nowed reticulin antibodies. Antibodies to chicken
bovine serum proteins were observed in 10 of 11
era positive for antibody to reticulin and in 6 of
sera negative for antibody to reticulin. These results establish a correlation between the antibody to reticulin and the antibodies to bovine and chicken serum proteins which may reflect a connection between the antigenic stimulation with reticulin to that with bovine or chicken serum proteins. The production of antibodies to reticulin and the production to bovine and chicken serum proteins can be elicited following the same type of antigenic stimulation. Reticulin, bovine, and chicken serum proteins are present in the same foods, usually given to infants during weaning. Therefore, the hypothesis that antibody to reticulin is produced as a consequence of the ingestion of reticulin is supported. The finding that 70%, 50%, 37% and 25% of the sera, resp. had antibodies to gluten, egg, albumin, potato, and milk, which do not contain reticulin, further strengthen this hypothesis.

7323 MEASUREMENT OF CELL PRODUCTION RATE IN THE HUMAN SMALL BOWEL. *(E.)* Wright, N. A.; Morley, A. R.; Appleton, D. R.; Marks, J. M.; Douglas, A. P.; Watson, A. J. (Dept. Pathol., Univ. Newcastle Upon Tyne, England). *Pathol. Microbiol.* 39(3-4):251-253, 1973.

Peroral duodeno-jejunal mucosal biopsies from 2 male patients (aged 61 and 39 yr; 1 had a history of rosacea and the other, dermatitis herpetiformis) were taken. Vincristine sulfate (0.045 mg/kg, i.v.) was injected to arrest mitosis at metaphase and 2.5 hr later a second mucosal biopsy was taken. Both biopsies from the patient with rosacea were normal in appearance, while biopsies from the patient with dermatitis herpetiformis showed characteristic histological changes of total villous atrophy indistinguishable from those of untreated celiac disease. The corrected cell cycle time was 45 hr in the control and 22 hr in the patient with villous atrophy. A 55-yr-old female with untreated celiac disease had a flat avillous mucosa. Several biopsies were taken after vincristine injection. The corrected cell cycle time was 21 hr. Thus it was concluded that linear collection of metaphases occurred in the human small bowel mucosa with the dosage of vincristine used and the duration of the observations. It is suggested that the observed increase in the mitotic index in the atrophic mucosa of untreated celiac disease or of dermatitis herpetiformis is due to increased rates of cell division.

7324 SUCCESSFUL TREATMENT OF COLLAGENOUS SPRUE WITH COMBINATION OF PREDNISOLONE AND GLUTEN-FREE DIET. *(E.)* Holdstock, D. J.; Oleesky, S. (Manchester Roy. Infirm., England). *Postgrad. Med. J.* 49(575):664-667, 1973.

The first case of collagenous sprue is reported in which the patient survives in good health. A 59-yr-old woman with anemia due to folate and iron deficiencies developed diarrhea and hypoalbuminemia with low urinary D-xylose excretion. After she was put on a gluten-free diet, the patient became critically ill with weight loss, steatorrhea, ascites, hypoproteinemic edema, reduced serum vitamin B_{12} levels, and evidence of protein-losing enteropathy. A jejunal biopsy showed subtotal villous atrophy, with very severe damage to enterocytes which were absent in some areas, and prominent subepithelial collagen. The patient failed to respond to a strict gluten-free diet, replacement therapy, and diuretics. Prednisolone (30 mg/day) produced considerable improvement, with regression of the ascites and edema and an increase in serum protein levels. A repeat jejunal biopsy showed only partial villous atrophy with no abnormal collagen, but a reduction in the dose of prednisolone to 15 mg/day resulted in hypoproteinemia, intestinal protein loss, skin lesions thought to be pemphigus erythematosus, and a skin biopsy showed vasculitis, Improvement occurred when the prednisolone dose was increased to 40 mg/day although improvement was interrupted by several grand mal seizures. After 4 months serum protein levels had returned to normal and the patient has remained well on a gluten-free diet, folic acid, and anticonvulsants. The prednisolone dose was cautiously reduced to 15 mg/day. These findings suggest that collagenous sprue may be a very severe form of adult celiac disease in which diet therapy must be combined with corticosteroids.

7325 GASTRIC ACID SECRETION AND INTESTINAL MALABSORPTION. *(E.)* Novis, B. H.; Bank, S.; Marks, I. N. (Groote Schuur Hosp., Cape Town, South Africa). *S. Afr. Med. J.* 47(26):1139-1142, 1973.

Gastric acid secretion was measured after pentagastrin stimulation or by the augmented histamine test in 47 patients (25 males and 22 females, aged 9-36 yr) with intestinal malabsorption caused by a variety of diseases. These included abominal lymphoma (10 cases), Crohn's disease (9), abdominal tuberculosis (7), blind loop syndrome (7), idiopathic steatorrhea (6), giardiasis (4), and folate deficiency (4). Controls consisted of 61 normal subjects, 230 hospital inpatients with no organic gastrointestinal disease, and 1149 patients with duodenal ulcers. In patients with intestinal malabsorption the mean basal and maximal acid outputs were 0.8 and 6.1 mEq/hr, resp. These values were significantly lower than those found in the 3 control groups. Of the patients with intestinal malabsorption, 50% had achlorhydria and 22% were achlorhydric after stimulation. Achlorhydria was present in only 10% of the normal controls and 1% of the patients with duodenal ulcers, and achlorhydria after maximal histamine stimulations was encountered in 8% of hospital inpatients with no evidence of gastrointestinal disease and in none of the normal controls or patients with duodenal ulcers. It is suggested that low gastric acid secretion in patients with intestinal malabsorption is caused by many factors resulting from malabsorption (weight loss, anemia, vitamin deficiencies, and hypoalbuminemia). However, no gastric biopsies were taken to determine whether or not these factors result in an increased incidence of atrophic gastritis or gastritis atrophy.

7326 THE BLIND-LOOP SYNDROME AND ITS VARIANTS. MICROBIOLOGIC ASPECTS OF DIAGNOSIS AND TREATMENT. *(E.)* Goldstein, F.; Mandel, R. J.; Schaedler, R. W. (Jefferson Med. Coll., Philadelphia, Pa.). *Am. J. Gastroenterol.* 60(3):255-264, 1973.

7327 EXOCRINE PANCREATIC FUNCTION IN CHROMIUM ENTEROPATHY: A STUDY OF THE FUNCTION AND COURSE IN SEVEN PATIENTS. *(Ger.)* Guller, R.; Kayasseh, L.; Stalder, G. A. (Dept. Intern. Med., Univ. Basel, Switzerland). *Dtsch. Med. Wochenschr.* 98(25):1268-1270, 1973.

7328 DISACCHARIDASE DEFICIENCIES. *(E.)* Newcomer, A. D. (Mayo Clin., Rochester, Minn.). *Mayo Clin. Proc.* 48(9):648-652, 1973.

7329 CONSEQUENCES OF BILE ACID MALABSORPTION. *(E.)* Hofmann, A. F. (Mayo Clin., Rochester, Minn.). *Mayo Clin. Proc.* 48(9):656-659, 1973.

7330 RADIOLOGICAL DIAGNOSIS OF LACTOSE INTOLERANCE IN CHILDREN WITH CHRONIC DIARRHOEA. *(E.)* Vazquez, B.; Amador, A. (William Soler Pediatr. Hosp., Havana, Cuba). *Acta Paediatr. Acad. Sci. Hung.* 14(1):51-61, 1973.

7331 GROWTH HORMONE IN MARASMUM DUE TO CEREBRAL DISEASE. *(E.)* Kerpel Fronius, E.; Gacs, G.; Hervei, C. (Semmelweis Univ. Med. Sch., Budapest, Hungary). *Am. J. Dis. Child.* 126(3):303-309, 1973.

7332 LOWE'S SYNDROME: MULTISYSTEMIC TRANSPORT ABNORMALITIES. *(Fr.)* Robillard, J. E.; Mongeau, J. G.; Morin, C. L.; Dallaire, L.; Massicotte, P. (St. Justine Hosp., Montreal, Canada). *Union Med. Can.* 107(7):1496-1501, 1973.

7333 RELATIONSHIP OF DIARRHEA TO MALDIGESTION AND MALABSORPTION. *(E.)* Phillips, S. F. (Mayo Clin., Rochester, Minn.). *Mayo Clin. Proc.* 48(9):660-662, 1973.

7334 CHRONIC DIARRHEA AND SEVERE MALABSORPTION SYNDROME IN INFANTS AFTER INFECTION WITH PATHOGENIC ESCHERICHIA COLI. *(Ger.)* Lucking, T.; Gruttner, R. (Pediatric Clin., Univ. Hamburg, Germany). *Monatsschr. Kinderheilk.* 121(7):376-379, 1973.

7335 TREATMENT OF DYSTROPHIC CHILDREN WITH MALABSORPTION. *(Ger.)* Szczepski, O. (Med. Acad., Poznan, Poland). *Monatsschr. Kinderheilk.* 121(7):379-381, 1973.

7336 CELIAC DISEASE IN THE ADULT: PATHOGENESIS AND CURRENT DIAGNOSTIC PROCEDURES. *(Sp.)* Garcia Jimenez, J.; Romero Gonzalez, R.; Pedreira Andrade, J. D.; Benasco Naval, C. (Francisco Franco Munic. Sanit., Barcelona, Spain). *Rev. Esp. Enferm. Apar. Dig.* 40(5):543-548, 1973.

7337 IRON ABSORPTION WITH TWO DIFFERENT TYPES OF DIET. *(Sp.)* Maisterrena, J. A.; Tovar Zamora, E.; Murphy, C. A. (Natl. Inst. Nutrition, Mexico City, Mexico). *Rev. Invest. Clin.* 25(1): 1-7, 1973.

7338 JEJUNAL DISACCHARIDES IN CHILDREN WITH SELECTIVE IgA DEFICIENCY. *(E.)* Savilahti, E.; Launiala, K.; Kuitunen, P. (Children's Hosp., Helsinki, Finland). *Scand. J. Gastroenterol.* 8(5):417-419, 1973.

7339 CONGENITAL MALTASE-SUCRASE AND MALTASE-ISOMALTASE DEFICIENCY IN AN ADULT. *(E.)* Mainguet, P.; Vanderhoeden, R.; Loeb, H.; Eggermont, E. (St. Pierre Univ. Hosp., Brussels, Belgium). *Digestion* 8(4):353-359, 1973.

7340 THE INFLUENCE OF THYROID HORMONE ON CALCIUM ABSORPTION FROM THE GUT IN RELATION TO URINARY CALCIUM EXCRETION. *(E.)* Lekkerkerker, J. F. F.; Doorenbos, H. (Univ. Hosp., Groningen, The Netherlands). *Acta Endocrinol.* 73(4):672-680, 1973.

7341 INTESTINAL ABSORPTION OF XYLOSE AND VITAMIN B_{12} LEVEL IN SERUM IN CHRONIC ALCOHOLISM. *(Pol.)* Kryszewski, A.; Niemiro, A.; Brandt, E.; Jarmuszczak, Z. (Acad. Med., Gdansk, Poland). *Pol. Tyg. Lek.* 27(40):1545-1547, 1972.

7342 CELIAC DISEASE-AN INBORN ERROR OF METABOLISM. *(E.)* Townley, R. R. W. (Roy. Children's Hosp., Melbourne, Australia). *Am. J. Dig. Dis.* 18(9):797-800, 1973.

7343 THE PATHOMORPHOLOGY OF WHIPPLE'S DISEASE. *(Pol.)* Kurasz, S. (Acad. Med., Bialystok, Poland). *Patol. Pol.* 23(3):373-378, 1972.

7344 WHIPPLE'S DISEASE IN A SEVEN-YEAR-OLD CHILD. REPORT OF A CASE. *(E.)* Barakat, A. Y.; Bitar, J.; Nassar, V. H. (American Univ. Med. Ctr., Beirut, Lebanon). *Am. J. Proctol.* 24(4):31-2 315, 1973.

7345 MALABSORPTION AND ITS CAUSES IN NATAL. *(E.)* Moshal, M. G.; Hift, W.; Kallichurum, S.; Pillay, K. (King Edward VIII Hosp., Durban, South Africa). *S. Afr. Med. J.* 47(25):1093-1103, 1973.

7346 THE GEOGRAPHICAL INCIDENCE OF LACTASE DEFICIENCY. *(E.)* Neale, G. (Roy. Postgrad. Med. Sch., London, England). *Pathol. Microbiol.* 39(3/4):238-247, 1973.

7347 MYCOPLASMA IN THE UPPER GASTROINTESTINAL TRACTS OF SOUTHERN INDIAN CONTROL SUBJECTS AND PATIENTS WITH TROPICAL SPRUE. *(E.)* Bhat, P.; Boulter, E. A.; Shanthakumari, S.; Kapadia, C. R.; Baker, S. J. (Christian Med. Coll. Hosp., Tamil Nadu, India). *Am. J. Clin. Pathol.* 59(6):825-828, 1973.

7348 LACTOSE INTOLERANCE IN CHILDHOOD. *(E.)* Gupta, B. M. (R. N. T. Med. Coll., Udaipur, India). *Indian Pract.* 26(3):153-155, 1973.

See also, 6706, 6761, 6838, 6850, 6869, 6974, 7205, 7213, 7214, 7266, 7279, 7286, 7454, 7534, 7537, 7775, 7929, 7950, 8024, 8140, 8186, 8204.

7349 INTENSITY AND PROXIMAL EXTENSION OF ACETYLCHOLINESTERASE ACTIVITY IN THE MUCOSA OF THE RECTOSIGMOID IN HIRSCHSPRUNG'S DISEASE. *(E.)* Elema, J. D.; de Vries, J. A.; Vos, L. J. M. (Univ. Hosp., Groningen, Netherlands). *J. Pediatr. Surg.* 8(3):361-367, 1973.

By staining for acetylcholinesterase activity, 51 consecutive rectal biopsies from infants and children were investigated for the presence of mucosal nerve fibers in order to evaluate the use of suction biopsies for diagnosis of Hirschsprung's disease. Acetylcholinesterase activity was increased in 8 of 9 patients (aged 2 months through 18 yr, 4 months) suffering from Hirschsprung's disease. This study suggest that the intensity and proximal extension of acetycholinesterase activity increases with age, and that mucosal activity does not extend as far proximally as in the submucous and intramuscular plexuses. No clear relation was found between length of the aganglionic segment and proximal extension of increased activity. From study of resected bowel segments, these 8 patients, it is concluded that false-negative findings in the rectal mucosa of patients with Hirschsprung's disease can be avoided by taking the biopsy immediately beyond the pectinate line. There were no false-positive findings.

7350 CELL PROLIFERATION IN RECTAL CARCINOMA AND RECTAL MUCOSA. A STATHMOKINETIC STUDY. *(E.)* Camplejohn, R. S.; Bone, G.; Aherne, W. (Dept. Pathol., Univ. Newcastle upon Tyne, England). *Eur. J. Cancer* 9(8):577-581, 1973.

A stathmokinetic technique was used *in vivo* to estimate the rate of cell proliferation in a group of 19 patients (14 male and 5 female, aged 52-81 yr) with carcinomas of the large bowel. This rate of proliferation was compared with that in normal rectal mucosa from 7 tumor-bearing patients (5 male and 2 male). The mean apparent cell cycle time of the tumors was 192 hr, and that of the normal rectal mucosa was 82 hr. The duration of mitosis was 2.3 hr in tumor cells and 1.2 hr in normal rectal mucosal cells. Speculative estimates of the rate of cell loss and of growth fraction in the tumors can be made by combining these results with those obtained with different kinetic techniques.

7351 BCG IN THE TREATMENT OF CARCINOMA OF THE COLON. *(E.)* Brown, C. R. (no affil.). *J. Abdominal Surg.* 15(9):186-187, 191, 1973.

Six patients with known carcinoma of the colon were treated by injections of Bacillus Calmette-Guerin vaccine. The vaccine was injected directly into metastatic tumors of the liver, lymph nodes, and surrounding tissues in 4 cases. In 2 patients with known metastatic lesions of the lung and liver the injections were made into subcutaneous tissue once a week for 4 weeks. All patients survived the treatment, although some of the resulting leukocytosis and toxic effects appeared rather frightening at times. All patients obtained a remission of the size and toxic effects of their metastatic carcinomas of the colon. Further research and longer observation periods will be necessary to determine if this effect is permanent or only a temporary remission due to the injection of Bacillus Calmette-Guerin vaccine.

7352 RADIOIMMUNOASSAY OF CIRCULATING CARCINOEMBRYONIC ANTIGEN. IMMUNO-PERCHLORIC EXTRACTION OF SERUM. *(Fr.)* Martin, F.; Klepping, C.; Guerrin, J. (Reg. Ctr. Cancer Control, Dijon, France). *Arch. Fr. Mal. App. Dig.* 61(12):725-733, 1972.

Using an original extraction technique (immunoprecipitation followed by perchloric acid extraction) and a modification of Farr's radioimmunoassay, circulating carcinoembryonic antigen levels were measured in serum from 231 patients with various diseases. These included cancers of the rectum (22), stomach (12), pancreas (10), esophagus (6), anus (3), liver (4), and biliary system (3); tumors not related to the gastrointestinal system (76); cirrhosis (24); peptic ulcers (10); viral hepatitis (7); colonic diverticulosis (6); polyps of the colon or rectum (5); enteritis (3); rectocolonic hemorrhage (2); intestinal ague (2); Crohn's disease (1); other gastrointestinal diseases (16); and nongastrointestinal diseases (19). High levels of carcinoembryonic antigen were detected in 11 of 22 patients with carcinomas of the colon. However, of 15 patients with no metastases, only 6 had increased circulating carcinoembryonic antigen levels. In addition, high concentrations of carcinoembryonic antigen were observed in some patients with various nongastrointestinal cancers and in patients with nonmalignant diseases (cirrhosis, colitis, etc.). These findings suggest that the value of this test for diagnostic purposes is questionable.

7353 FUDR AS AN ADJUVANT TO SURGERY IN CANCER OF THE LARGE BOWEL. *(E.)* Dwight, R. W.; Humphrey, E. W.; Higgins, G. A.; Keehn, R. J. (VA Hosp., Washington, D.C.). *J. Surg. Oncol.* 5(3): 243-249, 1973.

A group of 735 patients with carcinoma of the large bowel was studied in an effort to determine possible benefits of using 5-fluorodeoxyuridine as an adjuvant to surgical resection. Patients randomly selected to receive the drug were given 20 mg/kg (maximum dose 1.7 g) i.v. on the first 3 postoperative days. A second course of treatment, started 6 weeks later, consisted of 5 doses of 30 mg/kg (maximum 2 g) on successive days followed by 4 doses on alternate days of 15 mg/kg if toxicity did not appear. There was no significant difference between treated patients and controls in postoperative complications or 30 day mortality. The second course of chemotherapy was an apparent contributory factor in the death of 6 patients. Long-term follow-up studies showed no difference in survival between patients receiving the drug and those treated by surgery alone.

7354 ARTERIO-VENOUS ANASTOMOSES IN THE ANAL REGION WITH REFERENCE TO THE PATHOGENESIS AND TREATMENT OF HAEMORRHOIDS. *(E.)* Thulesius, O.; Gjores, J. E. (Central Hosp., Vaxjo, Sweden). *Acta Chir. Scand.* 139(5):476-478, 1973.

To determine whether arteriovenous shunting is present in hemorrhoids, oxygen saturation measurements and blood flow studies were made on 14 patients with hemorrhoids and on 5 controls with no major anal changes. Patients included 8 with primary idiopathic hemorrhoids and 6 with pronounced hemorrhoids during the last trimester of pregnancy. Oxygen saturation measurements were made on blood from the radial artery, cubital vein, portal vein, and anal vessels. Blood flow was determined in the anal ring after submucosal injection of physiological saline and 2 µg epinephrine and topical application of a vasoactive polypeptide (0.5 IU of ornithine-vasopressin). Significant differences were found between the oxygen content of venous blood and blood obtained by local puncture of hemorrhoids; anesthesia had no effect on the oxygen content. The consistent finding of high oxygen contents (mean 98%) in anal blood clearly indicates that arteriovenous shunts are a normal feature and supports previous anatomical evidence in favor of this view. Anal blood flow was reduced by administration of vasoconstrictors, presumably by the action of these agents on the inflow side of the vasculature since no dose-response relation was found for venous constriction. It is concluded that the following factors are involved in the pathogenesis of hemorrhoids: (1) rapid arterial inflow at high pressure, (2) local or distal venous outflow blockage, and (3) hormonal factors. It is suggested that drugs used to treat hemorrhoids should influence arterial supply vessels and not unduly affect the veins. This should decrease the perfusion pressure in the wide-bore capillary plexus and thereby prevent further distension. The primary objective of treatment should be to decrease local constriction of the venous outflow.

7355 LIPID-CHEMICAL DIFFERENCES BETWEEN HUMAN CANCEROUS AND ADENOMATOUS POLYPOUS TISSUES IN THE LARGE INTESTINE. *(E.)* Nakazawa, I.; Yamagata, S.; Watanabe, H. (Tohoku Univ. Sch. Med., Sendai, Japan). *Tohoku J. Exp. Med.* 110(1):23-32, 1973.

Biochemical differences between malignant neoplastic and benign growth were examined in 13 cases of cancer and 10 cases of adenomatous polyp of the large intestine. Cancerous or adenomatous polypous tissues were collected by biopsy or surgical operation. The total lipid was extracted from each tissue, and one part of each total lipid fraction was separated into triglyceride and phospholipid fractions by thin-layer chromatography. The fatty acid composition and the fatty acid content of each lipid fraction were measured by gas-liquid chromatography. Deviation rates representing the degree to which morbid tissue fatty acid content differed from that of control tissue were calculated for all lipid fractions. The deviation rate of $C_{14:0}$ was remarkably increased and that of $C_{20:4}$ was remarkably decreased in the cancerous cases, compared with the adenomatous polyp cases. When the ratio of the deviation rate of $C_{14:0}$ to that of $C_{20:4}$ was calculated in each case, more definite differences were recognized between the cancerous cases and the cases of adenomatous polyp. Namely, these ratios distributed between 2.404 and 4.125 in 7 cancerous cases, and between 0.564 and 1.856 in 8 cases of adenomatous polyp. Thus, using this ratio, it is possible to distinguish cancerous tissue from adenomatous polypous tissue.

7356 A NEW APPROACH TO COLONIC POLYPS. *(E.)* Wolff, W. I.; Shinya, H. (Beth Israel Med. Ctr., New York, N.Y.). *Ann. Surg.* 178(3):367-378, 1973.

From a group of 350 patients, 499 colonic polyps were endoscopically removed. The polyps ranged in size from 0.5 to 5.0 cm. The only complications were bleeding after removal of a wide based 3.5 cm villous adenoma high in the sigmoid colon (1 patient) and a minimally symptomatic perforation which occurred after resecting a sessile 2 cm polypoid carcinoma in the distal descending colon (1 patient). A surprisingly large number of polyps had both adenomatous and villous mucosal features. Malignant changes were noted in 6.8% of polyps; but clinically significant malignant change, manifested histopathologically as "invasive" cancer, was noted in only 3.4% of polyps. In 4 of the 16 patients involved, endoscopic resection was deemed to have accomplished complete removal. Bowel resections were performed on the remaining 12; of the 12 colons resected, 7 showed to residual tumor in the specimen. No mortality occurred during the endoscopic polypectomy. Pedunculated polyps were more readily resected than sessile types. Endoscopic polypectomy, since it is almost total biopsy, allows complete and unhurried pathologic study of the entire lesion. Separate colonic cancer is frequently associated with polyp formation and removal of the polyps should not obscure the possible early diagnosis of an associated cancer.

7357 BIOSTATISTICAL OBSERVATION ON CANCER OF THE COLON AND RECTUM. *(E.)* Garas, J.; Politis, A.; Michaelidis, G.; Besbeas, S.; Georgacas, G.; Evangelou, G. (St. Savas Hosp., Athens, Greece). *Int. Surg.* 58(9):633-634, 1973.

Adenocarcinoma of the colon and rectum was reviewed in 198 patients (aged 14-92 yr). In 154 (77.7%) of the patients, the carcinoma was located in the rectum and rectosigmoid junction. Of these 154, 110 underwent radical surgery, 31 had palliative excision, and 13 had a palliative colostomy or radiotherapy. In the remaining 44 patients (32.3%), the growth was in a loss of 15.9 kg. Histologic studies showed early membranous glomerulonephritis with thickening of glomerular basement membranes. Coarse granular deposits of IgG, IgA, IgM, and B_1C globulins were found along all glomerular capillary basement membrane. with occasional deposits in the mesangium, offering evidence of glomerulonephritis mediated by soluble immune complexes. Diffuse coarse granular deposits of CEA were also found along all glomerular capillary basement membranes. The combination of these deposits strongly suggests the renal lesion was instigated by soluble complexes consisting of CEA and anti-CEA antibody. The level of CEA in the blood of this patient was not particularly high, suggesting that the development of nephrosis may have been a complication of the patient's immune response to the neoplasm.

7358 SIGNIFICANCE OF CYTOLOGICAL EXAMINATIONS IN POLYPOSIS OF THE LARGE INTESTINE FOR DETECTION OF EARLY FORMS OF CANCER.

(Rus.) Chistova, N. M. (N. M. Petrova Res. Inst. Oncol., Leningrad, USSR). *Vopr. Onkol.* 19(6):42-48, 1973.

Washings from the mucosa of the large intestine were obtained from 21 patients with histologically confirmed polyposis of the large intestine, 13 with colonic cancer, and 4 with non-neoplastic lesions. Cytological examination of smears made from these washings provided evidence of malignant transformation or adenocarcinomatous changes in 7 patients with multiple polyps of the large intestine. Atypical cells, found in the intestinal epithelium in 2 patients, revealed that some of the polyps were undergoing proliferative changes. Although radiological and histological examinations were positive for cancer, no tumor cells were found in washings from a patient with a reticulum cell sarcoma of the submucosa. In 9 cases the benign nature of the polyps was confirmed. By examining intestinal washings a correct diagnosis was made in 10 of 13 patients with histologically confirmed cancer. In one of the 3 remaining patients atypical cells were found which were suggestive of cancer. In the second case tumor cells were not found in the smear although the pathological examination was positive; in a third patient a false-positive diagnosis was established. Use of this cytological method on washings from 4 patients with non-neoplastic disease gave diagnoses of inflammatory changes (2), diverticulosis (1), and chronic ulcerative proctitis. It is recommended that cytological examinations of washings from the large intestine be used to screen patients with intestinal polyps for early signs of cancer.

7359 PHYTOHAEMAGGLUTININ-INDUCED LYMPHOCYTE TRANSFORMATION IN PATIENTS BEFORE AND AFTER RESECTION OF LARGE INTESTINAL CANCER.

(E.) McIllmurray, M. B.; Gray, M.; Langman, M. J. S. (Gen. Hosp., Nottingham, England). *Gut* 14(7):541-544, 1973.

Lymphocyte responses to stimulation with phytohaemagglutinin were compared in 20 patients with large intestinal cancer, 10 patients whose large intestinal cancers had been removed, and in 30 age- and sex-matched control individuals. Thymidine uptake was much greater in normal cells than in cells of cancer patients. The thymidine uptake was slightly lower in lymphocytes from patients with unresectable tumors than in the other patients. Responses were unaffected by substituting normal for autologous plasma during incubation. Responses, however, were normal after tumor resection, suggesting that the defect in lymphocyte function is a reversible one, and is dependent on the presence of tumor tissue. In 2 patients the postoperative thymidine uptake was slightly lower than preoperative uptake, and this may suggest recurrent tumor.

7360 TORULOSIS OR CRYPTOCOCCOSIS OF THE COLON.

(Sp.) Valenzuela Casas, E. (Red Cross Hosp., Granada, Spain). *Rev. Esp. Enferm. Apar. Dig.* 40(5):523-532, 1973.

A 74-yr-old woman with a 2-yr history of gastrointestinal disorders developed signs of complete intestinal obstruction. On palpation, a mass, the size of an orange, was found at the right iliac fossa. At laparotomy about 3 liters of ascites fluid were obtained when the peritoneum was opened, and the mass was found to be intussusception of the cecum and ileum into the ascending colon. A right hemicolectomy was performed with an end-to-side ileotransverse anastomosis. The patient became afebrile, recovered uneventfully, and has no evidence of ascites or a recurrence 2 yr later. Histological examination of the resected intestine showed that the mass was a submucosal granuloma of the colon which was invaded with *Torula*; no neoplastic changes were found. A large number of *Torula* were also present in the feces. Sulfadiazine, Lugol's solution, and amphotericin B were administered p.o., and stool examinations were performed until no more *Torula* were found. Stools have been negative for *Torula* for about 2 yr.

7361 CARRAGEENAN-INDUCED SQUAMOUS METAPLASIA OF THE RECTAL MUCOSA IN THE RAT.

(E.) Fabian, R. J.; Abraham, R.; Coulston, F.; Goldberg, L. (Albany Med. Coll., N.Y.). *Gastroenterology* 65(2):265-276, 1973.

Degraded carrageenan, derived from *Eucheuma spinosum*, was administered to Sprague-Dawley rats as a solution in drinking water (5%; daily intake of carrageenan, 6-10 g/kg) or by stomach tube (0.5 or 5.0 g/kg/day). When the daily dose was 5 g/kg or more, the stools were soft to semi-fluid, and occult blood was detected in 3-7 days. Blood could occasionally be seen on the surface of the stool and on the anal margin. After 6 months, a gray-white coating of keratinizing stratified squamous epithelium was observed on the mucosal surface of the distal rectum. The epithelial transformation was preceded by acute and chronic inflammation, in which aggregation of macrophages in the he colon. Of these 44, 27 had radical resection, 10 ad palliative resection, 4 had radiotherapy, and 3 eceived systemic chemotherapy combined with radio- herapy or simple palliative measures. Rectal cancer ccurred more often in females (54.2%) than in males 46.8%). Colon cancer incidence was higher in males 57%) than in females (43%). Agricultural workers ad the highest incidence, 42% of rectal and 60% of olonic cancer, in males. The highest incidence of oth cancers was in the seventh decade of life. All atients except 4 were born in Greece, and the high- st incidence of both cancers was in Thessalia. Six onths had elapsed between the onset of symptoms and iagnosis in 40.5% of rectal cancer and 34% of colonic ancer patients. Rectal growths were located in the ower, middle, and upper third of the rectum in 37%, 5%, and 28%, resp. Neoplasms of colonic cancer were ocated in the sigmoid (52.5%), cecum (25.0%), as- ending (6.8%), splenic flexure (4.5%), descending 4.5%), and transverse (4.5%) segments. All colonic esions were adenocarcinomas except 5% which were ucous secreting carcinomas. The 5-yr survival was 8.6% for 58 patients with radical resection for rec- al carcinoma and only 10% for 20 patients on whom alliative resection had been performed. Of 18 co- onic carcinoma patients receiving radical resection, 4.4% survived 5 years. There were no 5-yr survivors n any other treatment groups.

362 COLONIC AND RECTAL COMPLICATIONS OF KIDNEY TRANSPLANTATION IN MAN. *(E.)* Bernstein, W. .; Nivatvongs, S.; Tallent, M. (Univ. Minnesota Hosp., inneapolis). *Dis. Colon Rectum* 16(4):255-263, 1973.

olonic and rectal complications developed in 13 of 02 patients who received 225 renal homografts. Ten f these 13 patients, who ranged in age from 12 days o 56 yr, died. The complications consisted of (1) epsis associated with necrotizing enterocolitis (3 ases); (2) sepsis associated with perforations of the owel or a sigmoid diverticulum (5 cases); (3) mas- ive hemorrhage from a cecal ulcer (2 cases); (4) ight-sided fecal impaction (2 cases); and (5) proc- algia due to ureterovesical obstruction (1 case). mmunosuppressive agents, particularly steroids, are robably one of the most important causes of necro- izing enterocolitis, because the incidence of this omplication decreased markedly after antilymphocyte lobulin was introduced the the doses of immunosup- ressive agents were reduced. Steroids are probably lso involved in the development of intestinal per- oration and cecal ulceration. The 2 patients who eveloped fecal impaction had been given antacids, hich have been implicated as a factor in the devel- oment of this complication, after surgery. Both f these patients had long histories of diabetes. fter his third kidney transplant a 15-yr-old boy eveloped the first reported case of proctalgia due o ureterovesical obstruction. Intractable pain was elieved by reanastomosing the ureter to the bladder. t surgery the obstruction was found to result from ecrosis and edema at the site of the anastomosis. easures recommended to prevent colonic and rectal omplications of kidney transplant surgery are (1) eduction of the doses of immunosuppressive agents, (2) avoidance of trauma to the colon during surgery, (3) detection and removal of areas of diverticulitis before kidney transplant surgery, and (4) careful monitoring of bowel function and administration of laxatives to counteract the constipating effects of antacids and cation-exchange resins.

7363 CHRONIC PHLEGMONOUS DIVERTICULITIS. *(E.)* Pheils, M. T.; Duraiappah, B.; Newland, R. C. (Repatriation Gen. Hosp., Concord, Australia). *Aust. N.Z. J. Surg.* 42(4):337-341, 1973.

Chronic phlegmonous diverticulitis, in which the phlegmon consisted of pericolic proliferation of dense fibrous tissue septa containing prominent foci of plasma cells, has been studied in 13 patients (11 males and 2 females, aged 43-77 yr), 7 of whom were over 70 yr old. In 8 cases there was no history of diverticular disease. In the other 5 cases, diverticular disease had been present for 4 to 10 yr. Resected sigmoid colon segments showed typical diverticula formation, mucosal redundancy, muscle thickening, and increased subserosal fat. Collagenous bands radiated from the bowel, incorporated subserosal adipose tissue, and formed adhesions to adjacent structures. In 8 of 13 specimens, chronic ulceration of diverticula was present; microperforation was seen in 5. The changes in chronic phlegmonous diverticulitis are due to prolonged contact between fecal material and tissue deprived of its protective epithelium. In 1 case Crohn's disease was coexistent. The most frequent symptoms were an episode of large bowel obstruction and a palpable abdominal mass. Barium enema revealed a long, narrowed, fixed segment of the sigmoid colon. A staged operative procedure is considered safer in the surgical management of these patients. Resection and anastomosis are suggested as the primary operation. A temporary transverse colostomy is then fashioned and not closed until all evidence of pelvic sepsis has subsided, usually several weeks later. Death occurred postoperatively in 2 patients (both of whom were over 70 yr of age), 1 due to pulmonary embolus and the other to cardiorespiratory failure. These 2 patients exemplify the risk of operation in this elderly group of patients.

7364 CARCINOEMBRYONIC ANTIGEN-ANTIBODY COMPLEXES IN A PATIENT WITH COLONIC CARCINOMA AND NEPHROTIC SYNDROME. *(E.)* Costanza, M. E.; Pinn, V.; Schwartz, R. S.; Nathanson, L. (New England Med. Ctr. Hosp., Boston, Mass.). *N. Engl. J. Med.* 289(10): 520-522, 1973.

A 57 yr old male had a "flu-like" syndrome 2 weeks after which edema developed, followed soon by bloody diarrhea. A lesion of the sigmoid colon was found. After the adenocarcinoma was resected, heavy proteinuria (24 g/24 hr) and a transient rise in serum creatinine (2.5 mg/100 ml) occurred. Neither prednisone (up to 120 mg/day) nor furosemide (40 mg/day) controlled these. Immunologic studies 1 1/2 months later showed the carcinoembryonic antigen (CEA) was 2.6 ng/ml. Prednisone was discontinued and furosemide increased (120 mg, 3 times/day) causing diuresis and lamina propria and submucosa was a prominent feature. Loss of mucosal glands, atrophy of the luminal epithelium, and replacement of the columnar epithelium by a stratified squamous epithelium took place in close association with these macrophage aggregates. Focal mucosal ulceration, followed by an acute inflammatory response, resulted in more intense proliferation of squamous epithelium involving the glands as well as the luminal epithelium. Most of the macrophages contained material assumed to be carageenan because it stained metachromatically with toluidine blue. A striking increase in histochemically demonstrable acid phosphatase activity paralleled the accumulation of this material. An etiological role is postulated for these macrophages in the pathogenesis of the colonic changes reported here. It is stressed that an evaluation of the extent to which degraded carrageenan is absorbed and stored in the reticuloendothelial system in humans is essential in evaluating the safety of this agent.

7365 MORPHOLOGICAL CHANGES INDUCED IN RECTAL CARCINOMAS BY PREOPERATIVE RADIATION THERAPY. *(Rus.)* Smirnov, N. M.; Simbirtseva, L. P.; Sneshko, L. I. (N. N. Petrov Sci. Res. Inst. Oncol., Leningrad, USSR). *Vopr. Onkol.* 19(6):49-56, 1973.

Histological changes induced in primary rectal tumors x-ray and ^{60}Co therapy were studied in 64 patients before and after exposure to a total of 3000 rads (five 600 rad sessions over a 10-day period). Of these patients, 21 (9 males and 12 females) were given preoperative x-ray therapy and 43 (18 males and 25 females) received preoperative ^{60}Co radiation. Histological changes induced in rectal tumors by radiation were similar in both groups of patients. They consisted in a decrease in the number of parenchymal cells with stromal cells predominating and small and large foci of necrosis. Extensive areas of granulation tissue were present on the surface of the tumors. Similar changes were found in regional lymph node metastases removed from 29 of these patients. No morphological changes were detected in normal tissue surrounding the tumors. Mitotic activity was reduced to the same extent in both groups. The number of abnormal mitoses was increased by 39% in patients given x-ray therapy and by 67% in those given ^{60}Co therapy; this difference is significant. The mitotic index, determined on tumors from 10 patients in each group, increased approximately 25% after x-ray and ^{60}Co therapy; this increase is considered too large to be due to chance.

7366 CELLULOSE DIETARY BULK AND AZOXYMETHANE-INDUCED INTESTINAL CANCER. *(E.)* Ward, J. M.; Yamamoto, R. S.; Weisburger, J. H. (Natl. Cancer Inst., Bethesda, Md.). *J. Natl. Cancer Inst.* 51(2): 713-715, 1973.

Male Fischer rats were fed either a low-residue semisynthetic diet or the same diet containing 20% and 40% of its bulk as cellulose. All animals were given injections of azoxymethane (14.8 mg/kg, s.c.) once a week for 10 weeks and held an additional 16 weeks. The food intake and weight of feces/day were proportional to the inert cellulose content of the diet. Most animals inoculated with the colon carcinogen had tumors in the intestinal tract. However, tumors in the small intestine were fewer than the average number of all intestinal tumors/rat, with the highest number on the semisynthetic diet and progressively lower numbers as the bulk of the diet increased. In the colon there were slightly more tumors/rat when the diet contained 20% cellulose. Thus azoxymethane-induced tumors in the small intestine were more sensitive to bulk and fiber content of the diet than were tumors in the colon. It is suggested that cellulose contributed inert bulk and bound the bile acids. This disturbed the enterohepatic circulation of some of the bile acids leading to increased secretion of these acids from the liver via the bile into the gut. The mechanism by which the increased bile flow and bile acids mediate changes in intestinal tumor incidence is unknown.

7367 BENIGN AND MALIGNANT MUCOCELE OF THE APPENDIX. HISTOLOGICAL TYPES AND PROGNOSIS. *(E.)* Aho, A. J.; Heinonen, R.; Lauren, P. (Dept. Surg., Univ. Turku, Finland). *Acta Chir. Scand.* 139(4):392-400, 1973.

A more precise, new histological classification was used in a study of 60 patients with mucocele of the appendix. The average follow-up ranged from 2.5-10 yr. The dominant subjective preoperative symptom was right lower abdominal pain (64%); 23% of the patients were asymptomatic. The histological groupings and prognosis of the mucocele were: Group I, retention cyst (11 cases), prognosis good. Group II, benign neoplastic mucocele (31), prognosis good. Group III, malignant invasive mucocele (7), true peritoneal pseudomyxoma associated with the condition. Prognosis poor, 5-yr survival rate, 25%. Group IV, mucocele with coexisting mucinous cystadenoma of the ovary (11). Prognosis fair, 5-yr survival rate, 60%. True peritoneal pseudomyxoma (epithelial components in the abdominal mucus on microscopy) was encountered only in the prognostically poor groups III and IV, representing 32% of the material. The treatment was generally appendicectomy and evacuation of the mucinous ascites from the abdominal cavity. The importance of examining a specimen of abdominal mucinous ascites and radical surgical treatment when possible in groups III and IV are stressed.

7368 INTUSSUSCEPTION OF THE APPENDIX. *(E.)* Down, R. H. L.; Bates, T. (Luton and Dunstable Hosp., Bedfordshire, England). *Br. J. Surg.* 60(8):619-620, 1973.

7369 DIVERTICULITIS OF THE COLON. *(Ger.)* Pross, E.; Kummerle, F. (Surg. Clin., Univ. Mainz, Germany). *Dtsch. Med. Wochenschr.* 98(22):1108-1112, 1973.

7370 POLYPOID LESIONS OF THE COLON AND RECTUM WITH SPECIAL REFERENCE TO EARLY DETECTION OF POLYPOID CANCER. *(E.)* Kobayashi, S.; Kasugai, T. (Aichi Cancer Ctr. Hosp., Nagoya, Japan). *Endoscopy* 5(3):117-120, 1973.

7371 SUBMUCOSAL CYSTS OF THE LARGE BOWEL. REPORT OF A CASE WITH CLINICAL REGRESSION. *(E.)* Kobayashi, S.; Kasugai, T. (Aichi Cancer Ctr. Hosp., Nagoya, Japan). *Endoscopy* 5(3):164-168, 1973.

7372 VASCULAR DISORDERS OF THE LARGE INTESTINE: EXPERIMENTAL FINDINGS AND CLINICAL CORRELATIONS. *(Fr.)* Rausis, C.; Robinson, J. W. L.; Mirkovitch, V.; Saegesser, F. (Dept. Surg., Univ. Lausanne, Switzerland). *Helv. Chir. Acta* 40(1/2): 295-305, 1973.

7373 CARCINOGENS AND CARCINOGENESIS IN THE COLON. *(E.)* Cole, J. W. (Yale Univ. Sch. Med., New Haven, Conn.). *Hosp. Practice* 8(9):123-130, 1973.

7374 ENTEROID CYST OF THE RECTUM. *(Fr.)* Paris, J.; Ribet, M.; Paris, J. C.; Heraud, M.; Houcke, M. (Univ. Hosp. Ctr., Lille, France). *Sem. Hop. Paris* 49(18):1300-1301, 1973.

7375 HEREDITARY SACROCOCCYGEAL AGENESIS WITH INCOMPLETE ANAL PERFORATION. MEGARECTUM IN CHILDHOOD AND PELVIC MENINGOCELE IN ADULTHOOD. *(Fr.)* Paris, J.; Laine, E. (Univ. Hosp. Ctr., Lille, France). *Sem. Hop. Paris* 49(18):1320-1322, 1973.

7376 PLASMACYTE SARCOMA OF THE CECUM WHICH APPEARED FOUR YEARS AFTER MULTIPLE MYELOMA. *(Fr.)* Guenel, J.; Dubigeon, P.; Guiheneuc, P.; Fonteneau, J. L. (St. Jacques Hosp., Nantes, France). *Sem. Hop. Paris* 49(22):1619-1622, 1973.

7377 TREATMENT OF ANAL FISSURES. *(Rus.)* Mun, N. V.; Grinberg, S. B. (Tselinograd Med. Inst., USSR). *Sov. Med.* 35(9):151-153, 1972.

7378 DEEP CYSTIC COLITIS. *(Fr.)* Auger, C.; Cadotte, M.; Fauteux, J. P. (Hotel Dieu, Montreal, Canada). *Union Med. Can.* 102(2):340-342, 1973.

7379 RESULTS FOR ABDOMINAL AND TRANSANAL SPHINCTER-PRESERVING PROCEDURES IN CANCER OF THE RECTUM AND SIGMOID. *(Ger.)* Deucher, F.; Blessing, H. (Cantonal Hosp., Aaru, Switzerland). *Schweiz. Med. Wochenschr.* 103(21):769-775, 1973.

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7477 NEW CONSIDERATIONS OF SHORT METHODS FOR RADIOLOGICAL EXAMINATION OF THE APPENDIX. *(Sp.)* Manzanos Gutierrez, J.; Leno Valencia, L. (no affil.). *Rev. Esp. Enferm. Apar. Dig.* 40(1):69-84, 1973.

7478 OBJECTIVE EVALUATION OF MUSCLE RIGIDITY IN THE ABDOMINAL WALL IN ACUTE APPENDICITIS. *(Rus.)* Barskii, A. V.; Derienko, V. S. (Kuibyshev Med. Inst., USSR). *Kazan. Med. Zh.* (3):30-32, 1973.

7479 ONE HUNDRED CASES OF SUSPECTED ACUTE APPENDICITIS: COMPARATIVE STUDY. *(Sp.)* Ferreira Montero, V.; Garcia Lisbona, J. R. (Jose Antonio Residence, Zaragoza, Spain). *Rev. Esp. Enferm. Apar. Dig.* 40(2):183-198, 1973.

7480 HODGKIN'S DISEASE OF THE COLON. *(E.)* Habib, M. A.; Donaldson, J. C.; Burningham, R. A. (US Naval Hosp., Philadelphia, Pa.). *South. Med. J.* 66(9):1067-1068, 1973.

7481 COLONIC MOTILITY DURING EXPERIMENTALLY INDUCED CONFLICTS IN SUBJECTS WITH DISEASES OF THE COLON. *(It.)* Trombini, G.; Lanfranchi, G. A.; Stegagno, L.; Bortolotti, M.; Miglioli, M. (Inst. Psychol., Univ. Bologna, Italy). *Boll. Soc. Ital. Biol. Sper.* 48(21):735-738, 1972.

7482 CANCER OF THE COLON. *(Sp.)* de Miguel, J. (no affil.). *Rev. Esp. Enferm. Apar. Dig.* 40(1):57-68, 1973.

See also, 6713, 6729, 6750, 6796, 6799, 6805, 6816, 6818, 6828, 6875, 6879, 6881, 6884, 6889, 6939, 7025, 7069, 7202, 7209, 7212, 7222, 7232, 7238, 7245, 7256, 7263, 7274, 7283, 7291, 7301, 7496, 7549, 7580, 7623, 8077, 8093, 8118, 8139, 8146, 8155, 8208.

LARGE INTESTINE

Ulcerative Colitis

7483 A CRITICAL EVALUATION AND ANALYSIS OF TOTAL COLECTOMY AND ILEORECTAL ANASTOMOSIS FOR PATIENTS WITH ULCERATIVE COLITIS. *(E.)* Vink, M.; Beerstecher, H. J. P. (Univ. Hosp., State Univ., Leyden, Netherlands). *Arch. Chir. Neerl.* 15(2):107-117, 1973.

A group of 73 patients (34 males and 39 females, aged 10-70 yr) with ulcerative colitis was studied. The disease was chronic-intermittent in 47, chronic-continuous in 15, and 11 patients needed operation during the initial attack. The time from the onset of symptoms till operation varied from immediate to 10 yr. The following local complications were diagnosed prior to operation: pararectal abscess (1), perianal fistula (4), hemorrhoids (6), pseudopolyps (35), stricture (4, 1 with carcinoma diagnosed during operation), dilation of the colon (4), perforation of the colon (4), and carcinoma (4). The following gastrointestinal complications were noted prior to surgery: nephrolithiasis (1), ureteral calculus (1), cirrhosis of the liver (2), and hepatic function disorders (6). Operations performed on this group consisted of partial colectomy (1); proctocolectomy (1); subtotal colectomy, ileostomy and terminal closure of rectum (29), ileorectal anastomosis (39), or ileorectal anastomosis and decompression ileostomy (3). The mortality rate for patients requiring immediate operation of an emergency nature was 13% in this series, whereas in the elective surgery group the mortality was nil. In cases where the rectum may be reasonably safely preserved, a primary intestinal anastomosis is practically always justified, provided that this anastomosis is situated retroperitoneally and is decompressed. It is mandatory that the patient submit to follow-up examinations once every 6 months and, after about 10 yr from the onset of symptoms, once every 4 months.

7484 THE METABOLISM OF SALICYLAZOSULPHAPYRIDINE IN ULCERATIVE COLITIS. I. THE RELATIONSHIP BETWEEN METABOLITES AND THE RESPONSE TO TREATMENT IN INPATIENTS. *(E.)* Das, K. M.; Eastwood, M. A.; McManus, J. P. A.; Sircus, W. (Western Gen. Hosp., Edinburg, Scotland). *Gut* 14(8):631-641, 1973.

Salicylazosulfapyridine metabolism was studied in 16 patients with ulcerative colitis. The acetylator phenotype was determined on hospital admission. Mean serum concentrations (μg/ml) (at steady state 8 ± 2 days in patients responding to treatment) of salicylazosulfapyridine, total sulfapyridine, and 5-aminosalicylic acid were 18.7 ± 12.8; 53.7 ± 23.1; and 1 ± 0.9 for slow acetylators and 17.6 ± 7.1; 31 ± 9.0; and 1 ± 0.9 for fast acetylators, resp. Urinary excretion of salicylazosulfapyridine, total sulfapyridine, and 5-aminosalicylic acids was 4.6% ± 3.1; 52% ± 9.6; and 22.3 ± 6.7% of the administered dose, resp. Serum total sulfapyridine concentration of 20-50 μg/ml appeared to coincide with clinical improvement in the absence of side effects related to salicylazosulfapyridine. No relation was seen with serum salicylazosulfapyridine, individual metabolites, or 5-aminosalicylic acid.

7485 INTESTINAL IMMUNOGLOBULINS IN ULCERATIVE COLITIS. *(E.)* Soltoft, J.; Binder, V.; Gudmand-Hoyer, E. (Gentofte Univ. Hosp., Denmark). *Scand. J. Gastroenterol.* 31(3):293-300, 1973.

Immunoglobulin determinations were made and immunoglobulin-containing cells were counted in 24 patients, aged 15-69 yr, with ulcerative colitis in the active phase. Studies were then repeated on 16 of these patients when their disease was inactive. In 3 patients only the rectum was involved; in 8, the rectum and most of the colon; and in the remaining 13, the whole colon was involved. Immunoglobulins were studied in jejunal and rectal biopsies, serum, jejunal juice, and whole saliva. The number of IgA cells was slightly increased in the jejunum, but IgA was decreased in jejunal juice in patients with active ulcerative colitis. In the rectum the area covered by IgA and IgG cells was increased. In inactive ulcerative colitis the jejunal mucosa was normal, but the IgA content of jejunal juice was decreased and the number of IgG cells in rectal biopsies was increased.

7486 METABOLISM OF SALICYLAZOSULFAPYRIDINE IN HEALTHY SUBJECTS AND IN PATIENTS WITH ULCERATIVE COLITIS. EFFECTS OF COLECTOMY AND OF PHENOBARBITAL. *(E.)* Schroder, H.; Lewkonia, R. M.; Price Evans, D. A. (Dept. Med., Univ. Uppsala, Sweden). *Clin. Pharmacol. Ther.* 14(5):802-809, 1973.

The metabolism of salicylazosulfapyridine in steady state was studied in 26 healthy volunteers, in 19 colitis patients (12 males and 7 females, aged 22-67 yr), 17 of whom had ulcerative colitis and 2 Crohn's disease, and in 10 subjects in whom the colon had been removed (ileostomized subjects). This study showed that the colon is the site of reductive cleavage of the azo linkage of salicylazosulfapyridine in man. Subjects with an intact colon excreted 60.5% of the dose in the urine as sulfapyridine metabolites which are formed after azo link cleavage. Ileostomized subjects excreted 7.1% of the dose of sulfapyridine metabolites. The metabolic pattern of sulfapyridine in healthy volunteers was similar to that in colitis patients. The serum concentrations of the various metabolites were measured. The levels of salicylazosulfapyridine on a dose of 2 g/day were similar in the 2 groups with a median of about 5 μg/ml. The serum concentration of total sulfapyridine ranged from 17 to 40 μg/ml in colitis patients and from 0 to 8 μg/ml in ileostomized subjects. Phenobarbital sodium (50 mg/night) was taken for 5 to 7 nights. Phenobarbital depressed urinary excretion of salicylazosulfapyridine by 18% in subjects with an intact colon, either by induction of a hepatic azo reductase or by enhancement of the biliary excretion of the drug. The proportions in urine of O-glucuronidized sulfapyridine were increased by 10% by acetylation of sulfapyridine. Phenobarbital apparently did not affect the metabolic pattern of salicylazosulfapyridine in ileostomized subjects.

7487 ADENOMATOUS EPITHELIUM, INTRAPITHELIAL ANAPLASIA, AND INVASIVE CARCINOMA IN ULCERATIVE COLITIS. *(E.)* Fenoglio, C. M.; Pascal, R. R. (Columbia Univ. Coll. Phys. Surg., New York, N.Y.). *Am. J. Dig. Dis.* 18(7):556-562, 1973.

A retrospective study of 328 biopsy and colectomy specimens from 240 patients with ulcerative colitis revealed the presence of adenomatous lesions in 37 cases and intraepithelial anaplasia in 8 cases, whereas invasive carcinoma occurred in 5 cases. The patients in whom invasive carcinoma or intraepithelial anaplasia was encountered usually had adenomatous lesions as well. Of the 5 cases of invasive carcinoma, 4 had foci of adenomatous epithelium elsewhere in the colon. Of the 6 cases in which the most severe lesion was intraepithelial anaplasia, 4 had additional foci of adenomatous epithelium. The estimated duration of ulcerative colitis prior to surgery was directly proportional to the severity of the neoplastic change. It is suggested that the origin of some carcinomas in ulcerative colitis is similar to the origin of colorectal cancer in the general population, i.e., from adenomatous epithelium.

7488 CIRCULATING IMMUNE COMPLEXES IN INFLAMMATORY BOWEL DISEASE.

(E.) Jewell, D. P.; MacLennan, I. C. M. (Radcliffe Infirm., Oxford, England). *Clin. Exp. Immunol.* 14(2):219-226, 1973.

Sera of 24 patients (13 males and 11 females, aged 30-60 yr) with ulcerative colitis and 18 patients (11 males and 7 females, aged 30-60 yr) with Crohn's disease were studied, for evidence of circulating immune complexes. Such sera produced significantly greater inhibition of antibody-induced cytotoxicity mediated by lymphocytes than did sera from 20 normal control subjects. Inhibitory activity of patients' sera showed a positive correlation with severity of disease, a high erythrocyte sedimentation rate and with severity of inflammation seen at sigmoidoscopy. Using gel filtration on Sepharose 6B, inhibitory activity was found in fractions of higher molecular weight than monomeric IgG but of lower molecular weight than IgM. These fractions contained IgG measured by immunodiffusion. Inhibition was not due to aggregated IgG molecules since no correlation was found between inhibitory activity and total IgG concentration. It is suggested that if the antigen-antibody complexes are formed in the mucosa, they may perpetuate the inflammatory response and thus play a part in the pathogenesis of inflammatory disorders of the gastrointestinal tract.

7489 SIMULTANEOUS MEASUREMENT OF ELECTRICAL POLARIZATION AND ELECTROLYTE TRANSPORT BY THE ENTIRE NORMAL AND INFLAMED HUMAN COLON DURING IN VIVO PERFUSION.

(E.) Rask-Madsen, J. (Glostrup Hosp., Copenhagen, Denmark). *Scand. J. Gastroenterol.* 31(3):327-336, 1973.

Steady-state perfusion of the entire colon with isotonic electrolyte solutions was used to investigate the transport of electrolytes by the normal and the inflamed colonic epithelium. Studies were performed on 11 healthy volunteers (5 females and 6 males, aged 16-64 yr) and on 10 patients (7 females and 3 males, aged 21-76 yr) with typical ulcerative colitis. At the time of the study 5 of the 10 patients had mild proctitis and 5 had severe ulcerative colitis. The absolute transport rates of electrolytes were reduced in ulcerative colitis, except for the secretion of potassium, which was increased in mild proctitis. The pattern of absorption was unaltered, however, even in severe ulcerative colitis. Studies of the polarization of mucosa from cecum to anus and bidirectional sodium fluxes suggest that the ability of mucosal cells to perform active transport may be impaired in ulcerative colitis, and that the reduced sodium absorption, at least initially, may be due to changed permeability characteristics. Regional differences in functional properties of the mucosa in the healthy colon were demonstrated by a gradual increase in the transmural potential difference from the cecum to the anus.

7490 STUDIES OF CARCINOEMBRYONIC ANTIGEN ACTIVITY OF WHOLE AND EXTRACTED SERUM IN ULCERATIVE COLITIS.

(E.) Khoo, S. K.; Hunt, P. S.; Mackay, I. R. (Walter and Eliza Hall Inst. Med. Res., Melbourne, Australia). *Gut* 14(7):545-548, 1973.

A microradioimmunoassay was used to detect carcinoembryonic antigen(s) (CEA) in whole serum and serum extracted with perchloric acid in 77 patients with ulcerative colitis, 2 of whom had coexisting colonic carcinoma, and 69 patients with carcinoma of the colon or rectum. Taking 5 ng/ml as the level of positivity, the CEA assay on whole serum showed positive results in patients with "active" ulcerative colitis (15 of 17) but not in those with "inactive" (0 of 23). Of the 69 cases of carcinoma of the colon or rectum, 66 were CEA-positive. In 2 colitis patients, with active colitis, CEA levels fell from 10 and 15 ng/ml to zero during remission induced by prednisolone and azathioprine. A positive result for CEA on extracted serum was associated with carcinamatous changes in ulcerative colitis in contrast to uncomplicated ulcerative colitis in which positive results were obtained only with whole serum.

7491 ULCERATIVE COLITIS: EPIDEMIOLOGICAL FINDINGS AND SYMPTOMS.

(Pol.) Ruzyllo, E.; Bartnik, W.; Bakowska, Z. (Ctr. Postgrad. Med., Warsaw, Poland). *Pol. Arch. Med. Wewn.* 49(5):443-448, 1972.

7492 ULCERATIVE COLITIS: ITS COURSE AND COMPLICATIONS.

(Pol.) Bartnik, W.; Bakowska, Z.; Ruzyllo, E. (Ctr. Postgrad. Med., Warsaw, Poland). *Pol. Arch. Med. Wewn.* 49(5):411-418, 1972.

7493 IMMUNOLOGICAL FEATURES OF IDIOPATHIC ULCERATIVE COLITIS AND CROHN'S DISEASE.

(E.) Perlmann, P.; Hammarstrom, S.; Lagercrantz, R. (Dept. Immunol., Wenner-Gren Inst., Stockholm, Sweden). *Rend. Gastroenterol.* 5(1):17-28, 1973.

7494 PSEUDOPOLYPOSIS IN ULCERATIVE COLITIS.

(Sp.) Zaragosi Moliner, J. (no affil.). *Rev. Esp. Enferm. Apar. Dig.* 40(5):515-522, 1973.

7495 THE SMALL INTESTINAL MUCOSA IN VARIOUS PHASES OF NONSPECIFIC ULCERATIVE COLITIS.

(Rus.) Survillo, O. N.; Pavel'eva, N. I.; Galushkiin, I. P. (Voronezh Med. Inst., USSR). *Arkh. Patol.* 34(10):42-45, 1972.

7496 ASSOCIATION OF ULCERATING COLITIS WITH COLON CARCINOMA. *(E.)* Terry, D.; Dodds, W. J. (Med. Coll. Wisconsin, Milwaukee). *Am. J. Gastroenterol.* 59(6):551-557, 1973.

7497 ACUTE ULCERATIVE COLITIS ASSOCIATED WITH CYTOMEGALIC INCLUSION VIRUS. *(E.)* Tamura, H. (Brown Univ., Providence, R.I.). *Arch. Pathol.* 96(3):164-167, 1973.

7498 PRACTICAL INTEREST OF THE STUDY OF THE MUCINS FOR THE DIAGNOSTIC OF PRIMARY COLITIS. *(Fr.)* Hemet, J.; Metayer, J. (C. Nicolle Hosp., Rouen, France). *Ann. Anat. Pathol. (Paris)* 17(3):389-392, 1972.

7499 BILE DUCT CARCINOMA IN CHRONIC ULCERATIVE COLITIS. *(E.)* Roberts-Thomson, I. C.; Strickland, R. G.; Mackay, I. R. (Hall Inst. Med. Res., Melbourne, Australia). *Aust. N.Z. J. Med.* 3(3):264-267, 1973.

7500 CONCOMITANT GASTRIC DISEASES IN CHRONIC ENTERCOLITIS AND THEIR TREATMENT. *(Rus.)* Davydich, L. N.; Khodykin, A. V.; Vashchenko, G. S.; Lukovskaya, O. L. (no affil.). *Vrach. Delo* (6):73-76, 1973.

See also, 6714, 7361, 7386, 7429, 8156, 8210, 8215.

PANCREAS

7501 CYSTADENOMA OF THE PANCREAS. A REAPPRAISAL OF ANGIOGRAPHIC FINDINGS. *(E.)* Pressman, B. D.; Asch, T.; Casarella, W. J. (Columbia-Presbyterian Med. Ctr., New York, N.Y.). *Am. J. Roentgenol. Radium Ther. Nucl. Med.* 19(1):115-120, 1973.

Markedly hypovascular cystadenomas of the pancreas are reported in 3 females, aged 17-40 yr. Duration of symptoms ranged from 2 weeks to 3 months and included midepigastric pain radiating to the back, mild to severe left upper quadrant pain, nausea, and vomiting. In 1 case the only symptom was an abdominal lump. The only abnormal biological test was a slightly elevated alkaline phosphatase level in 1 case. A pancreatic mass was demonstrated in each case arteriographically by displacement of contiguous major vessels and organs. In 2 cases the splenic vein obstruction was indicated by large retroperitoneal and omental venous collaterals. Histological sections of the surgically removed masses showed uniform cuboidal epithelium or multiple loculated cysts lined with columnar epithelium, each typical of benign pancreatic cystadenoma. The supposedly typical hypervascular arteriographic findings of pancreatic cystadenoma were absent in these 3 cases. In 2, there were no vessels within the tumor and the 3rd was hypovascular. Thus, arteriography can be used to differentiate between cystadenoma and pseudocyst only when the mass has the hypervascular pattern not seen in the pseudocyst. When a large spherical avascular or hypovascular pancreatic mass is demonstrated, differentiation must be made on clinical grounds.

7502 PREOPERATIVE ENDOSCOPIC CANNULATION OF PANCREATIC AND BILIARY DUCTS. *(E.)* Kozower, M.; Norton, R. A.; Raul, Jr., R. E.; Fawaz, K. A.; Miller, H. H.; Robbins, A. H.; Schimmel, E. M.; Sugarman, H. J.; Tomas, J. G. (New England Med. Ctr. Hosp., Boston, Mass.). *Ann. Surg.* 178(2):197-199, 1973.

Preoperative study of the pancreatic and biliary tracts by means of endoscopic cannulation of the papilla of Vater was attempted in 17 patients, 16 with jaundice and clinical symptoms of biliary tract obstruction, and 1 with suspected pancreatic carcinoma. In 4 patients surgical intervention was found unnecessary. The remaining 13 patients underwent exploratory surgery; the endoscopic procedure failed to provide a correct diagnosis in only 4 of these 13 patients. Cannulation of the papilla of Vater not only differentiated between surgical and medical jaundice, but also allowed the surgeon to determine the nature of the anatomical obstruction prior to operation and thereby choose the most appropriate procedure. Complications encountered in this procedure have been rare but do include bacteremia and elevated levels of serum amylase but no clinical evidence of pancreatitis.

7503 POLYARTHRITIS AND SUBCUTANEOUS NODULES ASSOCIATED WITH CARCINOMA OF THE PANCREAS.

(E.) Virshup, A. M.; Sliwinski, A. J. (VA Hosp., Washington, D.C.). *Arthritis Rheum.* 16(3):388-392, 1973.

The 14th reported case of polyarthritis associated with acinar cell carcinoma of the pancreas is presented. A 52-yr-old black man was admitted with lethargy, weakness, fever, and painful swelling of the right elbow and left pretibial area. He had a history of chronic alcoholism and a diagnosis of chronic pancreatitis with pseudocyst had been made 3 months earlier. Aspiration of the elbow yielded purulent fluid, and a diagnosis of septic arthritis was made. Antibiotics and antiinflammatory agents caused gradual improvement in the joint symptoms and reduced the fever. The test for rheumatoid factor was negative, but serum amylase and lipase levels were increased. An exploratory laparotomy revealed a pancreatic carcinoma with hepatic metastases. A recurrence of joint symptoms 6 months after admission failed to respond to treatment with colchicine, phenylbutazone, or aspirin. Joint aspiration yielded pus, but gram stain, acid-fast bacteria, routine culture, and fungal studies were negative. Courses of indomethacin, aspirin, and prednisone had no effect on joint symptoms. Shortly before death multiple areas of subcutaneous inflammation with purulent drainage developed on the patient's back, arms, and legs. Autopsy findings were consistent with the hypothesis that pancreatic lipase from hypersection by a functioning acinar cell tumor is released into the blood, causes autodigestion of subcutaneous and periarticular fat, and triggers a secondary inflammatory reaction. In unexplained cases of polyarthritis with subcutaneous nodules, pancreatic enzyme determinations should be performed, especially in alcoholics or in patients with known pancreatic disease.

7504 HYPERSECRETION OF ZYMOGEN GRANULES IN THE PATHOGENESIS OF CYSTIC FIBROSIS.

(E.) Blomfield, J.; Dascalu, J.; van Lennep, E. W.; Brown, J. M. (Roy. Alexandra Hosp. Children, Camperdown, Australia). *Gut* 14(7):558-565, 1973.

Examination of the submandibular saliva of 10 cystic fibrosis subjects (5 females and 5 males, aged 6-15 yr) and 10 controls confirmed the turbidity and elevated calcium, protein, and amylase concentrations of the cystic fibrosis secretions and precipitation of calcium and phosphate in a ratio consistent with hydroxyapatite. Electron microscopy revealed the centrifuged deposits of the cystic fibrosis saliva were composed predominantly of round or oval subcellular corpuscles. By comparison with submandibular gland, these corpuscles were identified as inclusion bodies (spherules) from within zymogen granules. Hydroxyapatite crystals formed on standing in the cystic fibrosis saliva. Polyacrylamide gel disc electrophoresis of the cystic fibrosis centrifuged deposits showed 5 bands, 1 of which, band 4 was more prominent in the deposit than in the supernatant gels. These results support studies showing elevated calcium and protein in cystic fibrosis exocrine secretions; simultaneous secretion of calcium and enzymes from salivary glands, stomach, and pancreas; and increased salivary secretion of calcium and protein in response to parasympathomimetic and sympathomimetic drugs. It is suggested that initial hypersecretion of calcium-containing zymogen granules leads to obstruction by insoluble products, with subsequent autolysis by trapped proteolytic enzymes, and eventual hypofunction.

7505 SPECIFICITY OF THE CORRECTION OF VITAMIN B_{12} MALABSORPTION BY PANCREATIC EXTRACT AND ITS CLINICAL SIGNIFICANCE.

(E.) Toskes, P. P.; Deren, J. J.; Fruiterman, J.; Conrad, M. E. (Walter Reed Army Inst. Res., Washington, D.C.). *Gastroenterology* 65(2):199-204, 1973.

Pancreatic extract (2g) increased the urinary excretion of labeled vitamin B12 from 2.0-15.4% in patients with pancreatic exocrine insufficiency, but had no effect when administered to normal volunteers or to patients with vitamin B_{12} malabsorption associated with pernicious anemia, bacterial overgrowth, or drug-induced disease. Pancreatic extract was useful in clarifying the cause of vitamin B_{12} malabsorption unresponsive to gastric intrinsic factor in 2 patients. One patient, a 54 yr old male, had a history of acute pancreatitis, but no clinical or laboratory evidence of chronic pancreatic exocrine insufficiency. In a 2nd patient, a 23 yr old female with pernicious anemia, vitamin B12 absorption was restored to normal only when pancreatic extract and gastric intrinsic factor were administered concomitantly. The demonstration of impaired bicarbonate output after secretin stimulation confirmed the presence of pancreatic dysfunction. Thus, pancreatic extract responsive-vitamin B_{12} malabsorption is specific for the vitamin B_{12} malabsorption associated with pancreatic disease, can occur in the absence of overt pancreatic disease, and may be the only indication of pancreatic dysfunction.

7506 INTRAVASCULAR CLOTTING IN PANCREATIC CARCINOMA.

(Ger.) Holub, G.; Fischer, M.; (Munic. Hosp., Wien-Lainz, Austria). *Med. Welt* 23(11):370-373, 1972.

A 60-yr-old woman who had been hospitalized 5 weeks before with pain in the upper abdomen was readmitted with a stroke. She developed localized cutaneous bleeding, melena, and mild jaundice. A diagnosis of disseminated intravascular coagulation was established by studying clotting factors. An increase in platelet count, fibrinogen, and factor V occurred within 2 days after institution of heparin infusions (250-300 IU/hr i.v. for 5 days), but the patient's general condition deteriorated, and she died 9 weeks after onset of symptoms. Autopsy revealed an adenocarcinoma in the body of the pancreas; this tumor had metastasized into the liver and pleural and peritoneal lymph nodes. Jaundice resulted from compression and invasion of the common bile duct by lumph node metastases. Large numbers of fibrin microthrombi were present in the liver and spleen, and thrombi were found in the portal and splenic veins, the many veins of the pelvis minor, and pulmonary artery. Hemorrhagic infarcts were present in the lower lobes of both lungs, both kidneys, the spleen, heart, and brain. No information was obtained to explain how the pancreatic tumor produced disseminated intravascular coagulation.

7507 DECREASED CHYMOTRYPSIN ACTIVITY IN CYSTIC FIBROSIS OF THE PANCREAS: ENZYME DEFICIENCY OR INACTIVATED ENZYME?

(Fr.) Neal, J. L.; Girgis, E. A.; Belmonte, M. M. (Biomedical Engineering Unit, McGill Univ., Montreal, Canada). *Union Med. Can.* 102(7):1465-1470, 1973.

To test the hypothesis that pancreatic enzyme deficiencies in cystic fibrosis are due to the presence of an inhibitor which acts on endogenous enzymes, endogenous chymotrypsin from a patient with cystic fibrosis was activated by affinity chromatography on agarose gel. After washing the gel free of chymotrypsin and equilibrating with distilled water, 10 ml of isotonic fecal extract from controls and patients with cystic fibrosis were applied to the column and columns were eluted with distilled water. Chymotrypsin activity in the eluant was compared with initial chymotrypsin activity by titrating the acid liberated by hydrolysis of N-acetyl-L-tyrosine methyl ester. Chymotrypsin activity in the eluant was significantly increased (10-100 times the original value) when fecal extracts or samples of duodenal juice from patients with cystic fibrosis were applied to the column. Only 55-75% of the original chymotrypsin activity was recovered when fecal extracts from controls were applied to the column. These findings and others reported in the literature disprove the hypothesis that the enzyme deficiency in cystic fibrosis is caused by obstruction of the pancreatic ducts, and they support the hypothesis that an inhibitor renders pancreatic enzymes inactive in cystic fibrosis.

7508 EFFECT OF MEDIUM CHAIN TRIGLYCERIDE ON FECAL CALCIUM LOSSES IN PANCREATIC INSUFFICIENCY.

(E.) Harrison, J. E.; McHattie, J. D.; Ligon, J. R.; Jeejeebhoy, K. N.; Finlay, J. M. (Dept. Med., Univ. Toronto, Ontario, Canada). *Clin. Biochem.* 6(2):136-140, 1973.

To assess the effect of medium chain triglyceride (MCT) on calcium absorption, a preliminary study was done on 4 patients with steatorrhea secondary to pancreatic insufficiency. In 3 subjects pancreatic enzyme therapy was discontinued throughout the investigation. In one subject the treatment with pancrelipase (6 capsules daily) was continued. Each patient was studied for 36 days on a constant low-fat diet. For the initial 12 days, 50 g of corn oil margarine was added to the basic diet; for the next 12 days, the margarine was removed from the diet, and for the last 12 days, 50 g of MCT fat spread was added to the diet. The MCT spread was tolerated by all patients. Aliquots of stool and diet were analyzed for fat. Based on preliminary results, and in agreement with reported data, the water-soluble MCT is more efficiently absorbed than long chain triglycerides in the absence of pancreatic enzymes but, in spite of the high percent absorption of MCT, no beneficial effect on calcium absorption was observed, either by calcium balance or by isotopic calcium studies. These results suggest that, with pancreatic insufficiency, defective calcium absorption is not due primarily to the formation of insoluble calcium soaps secondary to defective fat absorption.

7509 CYSTIC FIBROSIS OF THE PANCREAS. MORPHOLOGIC FINDINGS IN INFANTS WITH AND WITHOUT DIAGNOSTIC PANCREATIC LESIONS.

(E.) Oppenheimer, E. H.; Esterly, J. R. (Johns Hopkins Univ. Sch. Med., Baltimore, Md.). *Arch. Pathol.* 96(3):149-154, 1973.

Morphologic findings in 37 infants (21 males and 16 females, aged 2 hr to 2 yr) with a history of meconium ileus showed a wide diversity in the sites and severity of changes indicative of cystic fibrosis. No evidence of inspissated secretions, dilated acini or ductules, atrophy, interstitial fibrosis, nor fat were present in the pancreas of 10 patients, 9 of whom were less than 1 month of age. Anatomic lesions compatible with a diagnosis of cystic fibrosis were found in 34 of the 37 cases; the changes in the remaining 3 cases were suggestive or compatible with that disorder. There was no significant difference in the frequencies of extrapancreatic organ involvement between the group with pancreatic changes and those with a histologically normal pancreas. It is suggested that meconium ileus is always a manifestation of cystic fibrosis although there is variation in organ involvement.

7510 ADENOCARCINOMA OF THE PANCREAS IN FOUR SIBLINGS.

(E.) MacDermott, R. P.; Kramer, P. (Univ. Hosp., Boston, Mass.). *Gastroenterology* 65(1):137-139, 1973.

Pancreatic adenocarcinoma in 4 of 6 siblings is reported. In 2 brothers (aged 72 and 60 yr) and 1 sister, (aged 59 yr) the diagnosis was confirmed by autopsy or surgical biopsy. In another brother, (aged 59 yr) carcinoma of the pancreas was found at surgical exploration, but no biopsy or autopsy was obtained. None of the family had history of hereditary pancreatitis, pancreatic carcinoma, or any other type of carcinoma. There was no calcification of the pancreas on abdominal X-ray of the proband, nor was calcification reported in any of the other patients. The adenocarcinomas of the pancreas in this family appear to be an isolated occurrence of unknown cause.

7511 VASOACTIVE INTESTINAL PEPTIDE AND WATERY-DIARRHOEA SYNDROME. *(E.)* Bloom, S. R.; Polak, J. M.; Pearse, A. G. E. (Middlesex Hosp., London, England). *Lancet* (7819):14-16, 1973.

Of 6 patients with the watery-diarrhea syndrome (pancreatic cholera), all had raised plasma levels and/or high tumor content of vasoactive intestinal peptide, as measured by a specific radioimmunoassay. Positive immunofluorescence with vasoactive intestinal peptide antisera was obtained in 2 cases in which properly fixed tumor material was available. The known actions of vasoactive intestinal peptide accord well with the abnormalities found in the watery-diarrhea syndrome. The availability of a plasma-vasoactive intestinal peptide radioimmunoassay may enable the diagnosis to be made before tumor metastasis occurs. The association of vasoactive intestinal peptide with the watery-diarrhea syndrome supports the suggestion that this peptide is a hormone.

7512 INTRADUCTAL ACTIVATION OF PANCREATIC ZYMOGENS BEHIND A CARCINOMA OF THE PANCREAS. *(E.)* Allan, B. J.; Tournut, R.; White, T. T. (Univ. Washington Sch. Med., Seattle). *Gastroenterology* 65(3): 412-418, 1973.

Pancreatic secretions were collected from a 61 yr old male with carcinoma of the head of the pancreas who had a T-tube left in the pancreatic duct to relieve pain from ductal distention behind the tumor. Because the tumor totally blocked the duct to the left of the duodenum, there was no possibility of activation of the juice by enterokinase. The secretions collected were clear or slightly turbid, with a mean protein concentration of 2 mg/ml, containing no active proteases. Free chymotryptic activity was found in the juice 1 week postoperatively, but no active phospholipase A or elastase were present. Immediately after this patient had an attack of acute abominal pain. Pancreatic secretions became bloody and decreased in volume and protein output. Active chymotrypsin was present in all bloody specimens, but at lower specific activities than initially observed. When pain subsided, secretions were normal in flow rate and protein output. No free chymotrypsin was found. Suppression of the activation was associated with high levels of secretory trypsin inhibitor in the pancreatic juice. Later analysis showed that enzyme activity appears in the following order: carboxypeptidase, chymotrypsin, and phospholipase; then elastase and trypsin. A parallel secretion of pancreatic trypsin inhibitor with chymotrypsinogen and trypsinogen was also noted.

7513 CHEMOTHERAPY FOR CARCINOMA OF THE PANCREAS. *(E.)* Waddell, W. R. (Univ. Colorado Med. Sch., Denver). *Surgery* 74(3):420-429, 1973.

Inoperable carcinoma of the pancreas was treated with 5-fluorouracil (50 mg/kg, i.v., weekly) and sodium warfarin (p.o., in doses which lowered prothrombin time to 30% of normal) in 26 patients (14 males and 12 females, aged 33-89 yr), all of whom had adenocarcinoma of the usual type except 2, each of whom had papillary cystadenocarcinoma. An additional 13 patients (6 males and 7 females, aged 24-77 yr) with carcinoma of the pancreas received treatment with 5-fluorouracil and testololactone (50 mg, p.o., 3 or 4 times/day with meals). After 10 months time, 4 of these latter patients who were doing poorly had spironolactone (100 or 150 mg/day) added to the chemotherapy program, with a coincident reduction in testololactone to 100 mg/day. A comparison of the cumulative survival curves for the different forms of therapy shows highly significant advantages for those patients treated with 5-fluorouracil and testololactone or spironolactone. Side effects of 5-fluorouracil-testololactone administration were often severe nausea and vomiting which occurred in more than half the patients. Major infections occurred during therapy, presumably caused by immunosuppression. Peripheral edema was a frequent occurrence, though often transient. There were no recognizable complications of the 5-fluorouracil-spironolactone therapy other than hypoproteinemia and the associated fluid retention. Electrolyte depletion did not occur.

7514 EFFECT OF CHOLECYSTECTOMY ON EXOCRINE PANCREATIC FUNCTION IN MAN. *(Ger.)* Forell, M. M.; Otte, M.; Lechelt, B.; Roder, O.; Stahlheber, H.; Thurmayr, G. R.; Thurmayr, R. (2nd Med. Clin., Univ. Munich, Germany). *Dtsch. Med. Wochenschr.* 98(18):930-934, 1973.

Pancreatic function tests, performed before and after cholecystectomy on 16 patients (10 women and 6 men, aged 26-69 yr) and on 29 normal controls (16 men and 13 women, aged 23 60 yr), demonstrated that cholecystectomy had no effect on pancreatic secretion but did change the secretion kinetics. Preoperative determination of the bilirubin concentration in duodenal juice after i.v. injection of pancreozymin (1 Ivy dog U/kg) and secretin (1 Crick-Harper Raper U/kg) indicated that gallbladder function was normal in 9 and disturbed in 7 of these patients. After cholecystectomy patients with preoperative disturbances in gallbladder function secreted significantly less volume, bilirubin, and trypsin during the first 20 min after hormonal stimulation and significantly more bilirubin, trypsin, and lipase in the third 20 min period than before surgery. However, secretion over the entire 60 min period was the same before and after surgery. Cholecystectomy also had no effect on bilirubin or pancreatic secretion in patients who had normal gallbladder function preoperatively. Analysis of variance revealed no significant difference in 6 variables (volume, pH, and concentrations of bilirubin, bicarbonate, trypsin, and lipase) between these 16 patients preoperatively and the control group. Both before and after surgery pancreatic secretion was normal in 15 of the 16 patients. The single exception was a patient with a pancreatic pseudocyst.

7515 CLINICAL FORMS OF PANCREATIC CANCER. *(Fr.)* Bocquet, B. (Red Cross Hosp., Lyon, France). *Concours Med.* 95(16):2683-2695, 1973.

7516 CARCINOMA OF THE HEAD OF THE PANCREAS WITH LONG SURVIVAL AND A SUPERVENING CHOLEDOCHOLITHIASIS. *(Gr.)* Bladjas, G.; Gabrielides, C. G. (Surg. Clin., Aristotelian Univ., Thessalonika, Greece). *Iatriki* 21(1):144-147, 1972.

7517 MODIFIED MARSUPIALIZATION FOR CERTAIN PANCREATIC PSEUDOCYSTS. *(E.)* Miller, J. M. (no affil.). *J. Abdominal Surg.* 15(8): 141-143, 1973.

7518 SIMULTANEOUS DOUBLE CANCER: UTERINE CERVIX AND PANCREAS. *(Fr.)* Langeron, P.; Saout, J.; Muanza-Nkashama, E.; Beghin, B. (St. Philibert Hosp., Lille, France). *J. Sci. Med. Lille* 90(2):59-66, 1972.

7519 CROSS-CLASSIFICATION AND SURVIVAL CHARACTERISTICS OF 5,000 CASES OF CANCER OF THE PANCREAS. *(E.)* Baylor, S. M.; Berg, J. W. (Biometry Br., Natl. Cancer Inst., Bethesda, Md.). *J. Surg. Oncol.* 5(4):335-358, 1973.

7520 NEWER CONCEPTS OF PANCREATIC SECRETORY PATTERNS. PANCREATIC SECRETORY MASS AND PANCREATIC SECRETORY CAPACITY: PANCREATIC HYPERSECRETION. *(E.)* Dreiling, D. A.; Greenstein, A.; Bordalo, O. (Mt. Sinai Sch. Med., New York, N.Y.). *Mt. Sinai J. Med.* 40(5):666-676, 1973.

7521 ALPHA-1-ANTITRYPSIN DEFICIENCY IN A CHILD WITH CYSTIC FIBROSIS. *(E.)* Feigelson, J.; Pecau, Y.; Fagerhol, M. (no affil.). *Nouv. Presse Med.* 2(28):1899-1901, 1973.

7522 ECTOPIC PANCREAS. *(Sp.)* Gaspar Fuentes, A.; Campos Tarrech, J. M.; Fernandez Burgui, J. L.; Castells Tejon, E.; Ruiz Rossello, J.; Gomez Perez, J.; Armengol Miro, J. (Francisco Franco Munic. Sanitorium, Barcelona, Spain). *Rev. Esp. Enferm. Apar. Dig.* 39(3):255-268, 1973.

7523 PROTEASE INHIBITORS. *(Sp.)* Rodriguez Cuartero, A. (Dept. Intern. Med., Univ. Granada, Spain). *Rev. Esp. Enferm. Apar. Dig.* 39(3):331-336, 1973.

7524 PANCREATIC LESIONS IN ALCOHOLISM. *(E.)* Kojima, K. (Ctr. Pathol., Niigata Prefecture, Japan). *Acta Med. Biol.* 20(3/4):111-119, 1973.

7525 DIARRHEOGENIC TUMOR OF THE PANCREAS. *(E.)* Sato, T.; Komatsu, K. (Tohoku Univ. Sch. Med., Japan). *Am. J. Surg.* 126(3):425-429, 1973.

7526 PANCREATIC TRAUMA. *(Sp.)* de Juan y Martin, M. (Sanit., Logrono, Spain). *Rev. Esp. Enferm. Apar. Dig.* 39(4):389-410, 1973.

7527 SURGICAL THERAPY OF TUMORS OF THE HEAD OF THE PANCREAS AND PAPILLA. *(Ger.)* Liebeskind, R. (Munic. Hosp., Prenzlauer Berg, Berlin, Germany). *Z. Aertztl. Fortbild.* 66(3):164-169, 1972.

7528 A MODIFIED PANCREATICODUODENECTOMY. *(E.)* Powis, S. J. A.; Young, H. B. (no affil.). *Surg. Gynecol. Obstet.* 137(2):259-262, 1973.

7529 SYMPTOMATIC ANNULAR PANCREAS IN A 75-YEAR OLD MAN. *(E.)* Seliger, G.; Goldman, A. (New York Univ. Sch. Med., New York). *Am. J. Gastroenterol.* 60(2):185-190, 1973.

7530 LUNDH TEST IN THE DIAGNOSIS OF EXOCRINE PANCREATIC INSUFFICIENCY. *(E.)* Chawla, L. S.; Sehgal, A. K.; Verma, R. S.; Balakrishanan, V.; Chhuttani, P. N. (Postgrad. Inst. Med. Ed. Res., Chandigarh, India). *Ind. J. Med. Res.* 61(5):700-703, 1973.

7531 ANNULAR PANCREAS. *(Sp.)* Longo, O.; Richardet, E. (San Roque Hosp., Cordoba, Argentina). *Rev. Esp. Enferm. Apar. Dig.* 40(5): 549-552, 1973.

7532 INVAGINATION OF THE COMMON BILE DUCT, PANCREATIC DUCT, PAPILLA OF VATER AND DUODENUM BY AN AMPULLARY TUMOR. *(Fr.)* van Kemmel, M.; L'Hermine, C. (Munic. Hosp., Lille, France). *Sem. Hop. Paris* 49(18):1305-1308, 1973.

7533 ANGIOGRAPHIC ASPECTS OF CONTUSIONS OF THE PANCREAS. (FOUR CASES). *(Fr.)* Geindre, M.; Marty, F.; Fournet, J.; Baudain, P.; Champetier, M. (Univ. Hosp. Ctr., Grenoble, France). *Ann. Radiol.* 16(5-6):347, 1973.

7534 LACTASE DEFICIENCY IN CHILDREN WITH CYSTIC FIBROSIS OF THE PANCREAS. *(Ger.)* Niessen, K. H.; Schmidt, K.; Brugmann, G. (Child. Clin., Univ. Tubingen, Germany). *Klin. Wochenschr.* 50(7): 390-391, 1972.

7535 CARCINOMA OF THE PANCREAS MASKING CLINICALLY AS CENTRAL CARCINOMA OF THE BRONCHUS.

(Ger.) Weber, P.; Troger, J.; Ernst, H. (Steglitz Clin., Free Univ., Berlin, Germany). *Dtsch. Med. Wochenschr.* 98(29):1389-1391, 1973.

7536 ENDOSCOPIC CATHETERISATION OF THE PANCREATIC DUCTS. REPORT OF 160 CASES. *(Fr.)* Liguory, C.; Gouerou, H.; Monnier, J. P.; Chavy, A.; Conte, M. (St. Antoine Hosp., Paris, France). *Sem. Hop. Paris* 49(8):529-535, 1973.

7537 MALABSOPRTION AFTER PANCREATIC RESECTION: ITS REPONSE TO TREATMENT. *(Ger.)* Wanitschke, R.; Ewe, K.; Oyelowo, J. P. (Inst. Pharmacol. Toxicol., Univ. Saarlandes, Hamburg, Germany). *Dtsch. Med. Wochenschr.* 1212-1221, 1973.

7538 ASCITES AND PLEURAL EFFUSION DUE TO PANCREATIC DISEASE. *(Ger.)* Kummerle, F.; Mangold, G. (Surg. Clin., Univ. Mainz, Germany). *Dtsch. Med. Wochenschr.* 98:1423-1426, 1973.

See also, 6428, 6704, 6710, 6711, 6716, 6717, 6723, 6730, 6733, 6736, 6753, 6755, 6756, 6765, 6769, 6775, 6781, 6795, 6817, 6826, 6835, 6836, 6849, 7172, 7293, 7300, 7327, 7552, 7611, 7646, 7688, 7890, 7980.

PANCREAS

Pancreatitis

7539 MARKED HYPERLIPIDEMIA AND PANCREATITIS ASSOCIATED WITH ORAL CONTRACEPTIVE THERAPY. *(E.)* Davidoff, F.; Tishler, S.; Rosoff, C. (Beth Israel Hosp., Boston, Mass.). *N. Engl. J. Med.* 289(11):552-555, 1973.

Marked hyperlipidemia, recurrent episodes of abdominal pain and eventually pancreatitis developed in 2 women (aged 32 and 33 yr) receiving oral contraceptives. Initial and subsequent samples of blood drawn during admission with acute pancreatitis contained no chylomicrons. They have remained symptom free since contraceptive therapy was discontinued although mild elevations of endogenous triglycerides persist when they are on *ad lib* diets. In 4 other cases in the literature, massive hyperlipidemia developed during oral contraceptive therapy. Of these 4 patients 2 also had pancreatitis. Laparotomies were performed on 3 of the 4 pancreatitis patients for presumptive gallbladder disease. These experiences suggest caution in the use of oral contraceptives in patients with Type 4 hyperlipidemia, and should alert physicians to the possibility of pancreatitis secondary to hyperlipidemia in patients receiving these agents.

7540 INSULIN CONCENTRATION IN PORTAL AND PERIPHERAL VENOUS BLOOD AFTER ORAL GLUCOSE IN HUMAN PANCREATITIS. *(E.)* Erwald, R.; Hed, R.; Nygren, A.; Rojdmark, S.; Sundblad, L.; Wiechel, K. L. (Södersjukhuset, Stockholm, Sweden). *Acta Med. Scand.* 194(1-2):103-109, 1973.

Insulin and glucose concentrations in the portal and peripheral venous blood were determined in relation to oral glucose loads in 12 patients (11 males and 1 female, aged 27-61 yr) with acute (3) or relapsing (9) acute pancreatitis. A small insulin increase in the peripheral venous blood was not invariably accompanied by a small insulin increase in the portal blood, but was sometimes caused by a substantial reduction in the difference between the insulin level in the portal and peripheral venous blood. The fractional reduction in the difference between insulin in the portal and the peripheral venous blood tended to be higher at a high than at a low portal insulin level. The blood glucose concentration, however, did not influence the relation between portal and peripheral venous insulin concentrations.

7541 ACUTE PANCREATITIS IN PREGNANCY: A REVIEW OF 98 CASES AND A REPORT OF 8 NEW CASES. *(E.)* Wilkinson, E. J. (Med. Coll. Wisconsin, Milwaukee). *Obstet. Gynecol. Surg.* 28(5):281-303, 1973.

By analyzing statistics from 98 previously reported cases, it was found that in pregnancy the mortality from acute pancreatitis (37%) is much higher than that reported in nonpregnant individuals of similar ages (3.1% to 6.6%). Overall perinatal mortality was 37.9%. Although pancreatitis does not occur more frequently in the primigravida than in multiparous women, it is associated with 9% higher maternal and 13.5% higher perinatal mortalities. Eight previously unreported cases (aged 17-31 yr) of acute pancreatitis in pregnancy are presented. The rate of incidence during this study was 1:2,888 deliveries. Mortality was 50%. Of the 8, 3 were Negro and 5 Caucasian. Eight infants survived, including 1 set of twins. All but 2 patients were multiparous. Acute abdominal pain was the presenting symptom in 6 of the 8; fever was present in 7. All developed the disease in either the third trimester (4) or during the postpartum period (4); in each group the mortality was 50%. A clinical diagnosis was made in 7 cases. Biliary tract disease was present in 3. Preeclampsia was associated with the pancreatitis in 4 cases. Tetracycline was administered to 2 patients, both of whom died. Chlorothiazides had been administered to 2 other patients before the onset of pancreatitis. Pancreatic pseudocysts were noted in 2 patients, both of whom survived. Profound anemia occurred in 3, of whom 2 died. Marked hyperglycemia (glucose levels up to 1,230 mg/100 ml) occurred in 2 cases; proteinuria occurred in 7 of the 8. Treatment is aimed at preventing and treating shock, suppressing pancreatic secretion, relieving pain, preventing and treating infection, and diagnosing and treating surgical complications.

7542 INSULIN LEVELS IN ACUTE EXPERIMENTAL PANCREATITIS IN DOGS. *(E.)*

Satake, K.; Carballo, J.; Appert, H. E.; Howard, J. M. (Hahnemann Med. Coll., Philadelphia, Pa.). *Surg. Gynecol. Obstet.* 137(3):467-471, 1973.

Intraductal injection of autologous bile in dogs induced acute pancreatitis. The mean arterial pressure decreased gradually but was maintained about 100 mm of mercury under constant infusion of saline solution. Plasma amylase, lipase, and trypsinogen levels rose significantly, but elastase decreased gradually. Plasma insulin levels rose significantly 30 min after onset of the pancreatitis and then gradually decreased but remained above normal levels throughout 5 hr of observation. Glucose concentrations also rose within 30 min after onset of pancreatitis but fell below the control levels at the end of the experiments. The changes in insulin and glucose levels in thoracic duct lymph were less than those found in the portal blood. High insulin and glucose levels have been observed in ascitic fluid. This study confirms that most of the excess insulin found after the onset of experimental pancreatitis results from its release from pancreatic storage as a direct consequence of cell disruption. If due to intrinsic disease, the pancreas is not able to produce new insulin after the initial injury, which may contribute to the diabetic-like feature occasionally observed in acute pancreatitis.

7543 NECROSIS OF THE SPLEEN IN THE COURSE OF CHRONIC PANCREATITIS. *(Fr.)*

Blery, M.; Coulbois, J.; Gaux, J. C.; Bismuth, V. (Ambroise Pare Hosp., Boulogne, France). *Nouv. Presse Med.* 2(14):915-917, 1973.

A 53-yr-old man with a 3-yr history of episodes of pain in the left abdomen and thorax was hospitalized with a pleural effusion on the left. No evidence of a neoplasm or tuberculosis was found. A barium enema showed stenosis immediately below the left angle of the colon and a regular, round shadow which projected from the large curvature of the stomach. Celiac and mesenteric arteriography revealed compression of the splenic artery; its branches travelled upward to irrigate a mass resembling a tumor. This tumor was well supplied with blood vessels. A normal spleen was not visualized. Laparotomy showed that the spleen was involved in an inflammatory process which included the tail of the pancreas, the left adrenal, and the left angle of the colon. The colon was freed and the inflammatory block resected. A subcapsular hematoma of the spleen was found which had thickened, inflamed walls. A mass of spleen tissue the size of an orange was separated from the capsule by lysed blood. Histology confirmed the diagnosis of a hematoma and showed chronic pancreatitis in the tail of the pancreas.

7544 GLUCAGON THERAPY IN ACUTE PANCREATITIS. *(E.)*

Condon, J. R.; Knight, M.; Day, J. L. (St. Mary's Hosp., Eastbourne, London, England). *Br. J. Surg.* 60(7):509-511, 1973.

Glucagon (1 mg i.v. followed by infusion of 1-1.5 mg every 4 hr for 24-96 hr) was administered to 30 patients with acute pancreatitis. Pancreatitis was classified as severe in 10 cases because of severe clinical shock, plasma calcium levels of less than 7.0 mg/100 ml, and hemorrhagic pancreatitis diagnosed either at surgery or by detection of methemalbuminemia. Within 12 hr after initiation of glucagon therapy, pain was relieved in 90% of the patients with severe and in 95% of those with nonsevere pancreatitis. Plasma amylase activities decreased during glucagon infusion in all but 1 patient. In contrast to recently published British studies which reported mortalities of 22% and 26%, only 2 of these 30 patients (7%) died.

7545 METASTATIC CARCINOMA TO THE PANCREAS. ANOTHER CAUSE FOR ACUTE PANCREATITIS. *(E.)*

Levine, M.; Danovitch, S. H. (Washington Hosp. Ctr., Washington, D.C.) *Am. J. Gastroenterol.* 60(3):290-294, 1973.

A 45-yr-old male was hospitalized with superior vena caval obstruction. Inoperable oat cell carcinoma involving the right upper lobe of the lung was found and radiated. Rehospitalization 6 months later for abdominal pain and breathlessness revealed persistent hyperamylasemia and transient hyperlipasemia in the absence of renal failure or hypercalcemia. Laboratory tests were normal with the exception of the alkaline phosphatase which was elevated to 3.2 Bessey-Lowry U on one occasion. Autopsy showed that metastatic oat cell carcinoma of the lung had replaced nearly the entire pancreas with spread to the brain, bone, and liver. Pancreatic fibrosis, ductular ectasia sparing of the islets of Langerhans, minimal inflammatory exudate, and replacement of acinar cells by metastatic oat cell carcinoma were observed. In a second case, a 48-yr-old male suffering from breathlessness, radiography showed a left lung lesion. An inoperable bronchogenic carcinoma of the left lower lobe was revealed at thoracotomy, and palliative radiotherapy was administered. After 6 months, weakness, weight loss, and epigastric fullness were noted. One month later laboratory tests showed elevations of alkaline phosphatase, SGOT, SGPT, and bilirubin. Autopsy showed pancreatic metastasis with accompanying duodenal and common duct obstruction along with metastasis to the bone, kidney, and liver. Pancreatic fibrosis, ductural ectasia, fat necrosis, and extensive infiltration with acute and chronic inflammatory cells accompanied the metastatic bronchogenic carcinoma. In neither of these cases was there any evidence that drugs, alcohol abuse, or cholelithiasis could be implicated as a cause of the pancreatitis.

7546 ROENTGENOLOGIC DIAGNOSIS OF PANCREATIC ABSCESS. *(E.)* Tylen, U.; Dencker, H. (Univ. Hosp., Lund, Sweden). *Acta Radiol. (Diagn.)* 14(1):9-16, 1973.

Records of 21 patients diagnosed as having a pancreatic abscess were re-examined to assess the value of the different roentgenologic methods used in establishing the diagnosis. Roentgenography of the chest, performed on 10 patients, showed left pleural effusion in 2 and left or right basal atelectasis in 3. Roentgenography of the abdomen showed changes in 4 of the 8 examined. Gas bubbles in an abscess were evident at the right iliac fossa in 1 patient and in the left flank in another. Expansive lesions in the upper part of the abdomen were detected in 2 patients, 1 of whom also had distended transverse colon and the other a displaced stomach. Barium meal exams revealed abnormalities in 8 of 9 patients: in 6 patients the stomach was moved forward by a retrogastic expansive lesion and a minor deformity of the duodenal loop was present in the other 2. Selective visceral angiography demonstrated the pancreatic abscess in all 9 patients examined. In 7 of these 9 displacement of the splenic, left gastric and intestinal arteries occurred; the degree of displacement was often pronounced and corresponded to the size of the abscess at operation. Smooth and rather small arterial stenotic lesions, most frequent in the splenic artery, were noted in 8 patients. Increased tortuosity and a slightly irregular lumen were found in pancreatic arteries in 9 patients and in intestinal arteries, mainly the middle colic artery, in 6. Venous lesions were evident in 7 patients. Selective visceral angiography appeared the most reliable method and is recommended for the early diagnosis of very small pancreatic abscesses.

7547 NEPHROSIS, STEROIDS, PANCREATITIS, AND DIABETIC KETOACIDOSIS. *(E.)* Kobayashi, A.; Utsunomiya, T.; Horino, M.; Ohbe, Y.; Hata, J. (National Children's Hosp., Tokyo, Japan). *Am. J. Dis. Child.* 125(5):726-729, 1973.

A 9 1/2 yr-old boy was given betamethasone (5 mg/day) for nephrosis. His condition improved, but reduction of the dose to 1.5 mg/day caused a relapse which was treated with betamethasone (2 mg/day) and cyclophosphamide (50 mg/day). Due to varicella in the ward, cyclophosphamide therapy was discontinued. After 11 weeks steroid-induced glycosuria was diagnosed. The betamethasone dose was reduced and cyclophosphamide (75 mg/day) reinstituted. After 2 weeks SGOT and SGPT activities were increased. The patient then went into shock, and a diagnosis of diabetic ketoacidotic coma was made. Appropriate treatment caused improvement, but severe oliguria supervened and the patient died after an episode of gastrointestinal bleeding. Autopsy revealed acute hemorrhagic pancreatitis with widespread peripancreatic fat necrosis and patchy obstruction of the pancreatic ducts. This obstruction may have been produced by ductal epithelial proliferation, by an increase in viscosity of pancreatic secretion, or both. This obstruction may be a primary factor in the pathogenesis of steroid-induced pancreatitis. The role of cyclophosphamide is unclear, but it may also have been a major cause of pancreatitis. The chronically depressed immune response of patients receiving immunosuppressants may facilitate the progression of pancreatitis by the inability to produce antibodies to the antigenic component of this disease.

7548 HYPERLIPEMIA AND PANCREATITIS. *(E.)* Tasman-Jones, C.; Abraham, A. (Auckland Hosp., New Zealand). *Am. J. Dig. Dis.* 18(9):767-772, 1973.

Case reports are presented for 2 men, aged 48 and 34 yr, resp., with hyperlipemia associated with acute pancreatitis. The first patient had a history of increased alcohol intake, while the second had an excessive intake of carbohydrate and diabetes mellitus. Hyperlipemia improved when the first patient discontinued alcohol and the second stopped eating a high carbohydrate diet. Post-heparin lipoprotein lipase was initially elevated in both patients but subsequently decreased to values in the normal range when dietary abnormalities and pancreatitis had been corrected. In the first patient the activity of this enzyme increased again with the development of a pancreatic cyst; the cyst disappeared without surgery. It is possible that increased lipoprotein lipase activities were caused by a combination of lipoprotein lipase leached out of tissues as a result of triglyceridemia of relatively long duration and heparin-released lipoprotein lipase from the capillary endothelium. The first patient, who had marked hypercholesterimia and hypertriglyceridemia, had a substance in his serum which inhibited lipoprotein lipase activity in the post-heparin plasma of a normal subject. Since inhibition was completely abolished by heat and was reduced from 60% to 40% by dialysis, this inhibitor is probably a protein which is released from necrotic pancreatic tissue.

7549 EFFECTS OF PANCREATITIS ON THE SMALL BOWEL AND COLON: SPREAD ALONG MESENTERIC PLANES. *(E.)* Meyers, M. A.; Evans, J. A. (New York Hosp., Cornell Univ., New York). *Am. J. Roentgenol. Radium Ther. Nucl. Med.* 119(1):151-165, 1973.

Pancreatitis was studied in 3 patients (2 males and 1 female, aged 47-76 yr). Diagnoses included stricture of the distal ascending colon secondary to suppurative pancreatitis, stricture of the splenic flex- ure secondary to traumatic pancreatitis, and mala- sorption and jejunal atrophy secondary to chronic ancreatitis. Pancreatitis extends along the mesen- teric planes of the transverse mesocolon to the large intestine and to the jejunum, ileum and cecum via he small bowel mesentery. In the large intestine, he transverse colon and in particular the splenic lexure are most commonly involved. The distal scending colon may be involved by a duodenal fistula. n the small bowel, the inflammatory process may electively involve jejunal loops or may progress own the mesentery to localize in the ileocecal rea. Malabsorption may result from pancreatitis n the small bowel. The lesions produced range from ransient spasm to the development of obstructive trictures and remote exudative abscesses.

550 HEMODYNAMIC AND METABOLIC EFFECTS OF VASOPRESSIN IN ACUTE HEMORRHAGIC PANCREATITIS. *E.)* Pissiotis, C. A.; Van Meter, S. W.; Condon, R. (Univ. Iowa Coll. Med., Iowa City). *Eur. Surg. es.* 5(1):64-72, 1973.

ute hemorrhagic pancreatitis was induced in adult ngrel dogs by injecting into the main pancreatic ct a mixture of 6 ml blood, 40,000 units crystal- ne trypsin and 4 ml bile, under a pressure of more an 140 mm Hg. Cardiac output was relatively stable normal controls whereas decreases of 30% at 30 min d 50% at 120 min after induction of hemorrhagic pan- eatitis were recorded. The cardiac output was high- in vasopressin-treated animals (0.012 units/kg/ n). Aortic pancreatic blood flow fell to 58% of seline in animals with pancreatitis, with a lesser crease in those treated with vasopressin. Portal nous pressure increased immediately on pancreatitis duction, but was lower in vasopressin treated ani- ls. The arterial-pancreatic venous oxygen gradient pancreatitis fell, but was higher in vasopressin eated animals. Serum amylase was higher in pancre- itis groups than in controls. There was no differ- ce in serum amylase levels between treated or un- eated animals up to 2 hr after induction of pancre- itis. It is suggested that the inflamed pancreas treated animals extracts more oxygen supplied to through a higher perfusion pressure and flow. se results indicate that the vasopressin effect pancreatitis is dependent largely on systemic re- nses to the drug. Since there was no significant difference in pancreatic blood flow between treated and non-treated animals, if pancreatic blood flow was expressed as fraction of cardiac output, pancreatic perfusion is chiefly dependent on cardiac output.

7551 HEPATIC LESIONS IN ACUTE NECROTIZING PANCREATITIS. *(Fr.)* Camilleri, J. P.; Rettori, R.; Chiche, B.; Olivier, C. (Hotel Dieu, Paris, France). *Arch. Fr. Mal. App. Dig.* 62(5): 369-378, 1973.

Histological examinations of the liver were performed at autopsy on 30 nonselected patients (16 men and 14 women) who died of acute necrotizing pancreatitis. Hepatomegaly was present in 21 cases and hepatic atrophy in 1. In addition to preexisting liver disease (chronic cholangitis secondary to choledocholithiasis in 1, micronodular cirrhosis in 1, and chronic liver disease with portal cirrhosis which was alcoholic and/or nutritional in origin in 3), fatty liver was diagnosed in 20 patients, degenerative lesions without necrosis in 10, liver cell necrosis in 11, cholestasis in 10, siderosis in 3, inflammatory cell infiltration in 18, and distension of the sinusoidal bed in 21. Clinical and/or biological signs of liver disease were found in 11 cases, while liver disease was diagnosed only at autopsy in 12 cases. Liver cell necrosis appeared to be correlated with jaundice which developed 2-5 days after the onset of pancreatitis. It is suggested that hepatic lesions could be secondary to shock in acute necrotizing pancreatitis.

7552 THE CALCIUM CONCENTRATION IN PANCREATIC SECRETION IN CHRONIC PANCREATITIS AND CARCINOMA OF THE PANCREAS. *(E.)* Warwick, R. R. G.; Tothill, P.; Percy-Robb, I. W.; Shearman, D. J. C. (Roy. Infirm. Edinburg, Scotland). *Scand. J. Gastroenterol.* 31(3):301-305, 1973.

Calcium concentrations in the duodenal aspirate during a standard secretin stimulation test was measured in a series of 21 patients with a normal pancreas, 14 patients with pancreatitis and 7 patients with pancreatic carcinoma. The calcium concentrations were significantly higher in the two abnormal groups than in the normal group. The findings confirm those of previous work and it is suggested that estimation of calcium concentration of duodenal aspirate may be a useful test for pancreatic disease. Because of the low volumes of duodenal aspirate produced by the pancreatitis and carcinoma subjects, however, there was no significant difference in total calcium ouput between the normal and abnormal groups. When [^{47}Ca] calcium chloride (10 μCi, i.v.) was injected, [^{47}Ca] appeared rapidly in the duodenal aspirate in normal subjects. Thus it is concluded that, for normal subjects, the calcium content of the duodenal aspirate is derived from the plasma calcium via a small pool. In 1 chronic pancreatitis patient there was some evidence of an increase in the pancreatic pool of calcium.

7553 ACUTE PANCREATITIS IN COXSACKIE B INFECTION.

(E.) Ursing, B. (Univ. Hosp., Lund, Sweden). *Br. Med. J.* 3(5879):524-525, 1973.

Two cases of acute pancreatitis in Coxsackie B infection are discussed. A 27-yr-old woman fell ill with pyrexia, arthralgia, and pain in the right chest. On hospital admission she had exanthema and severe abdominal pain. During the following week she developed a fulminant picture of acute pancreatitis. Bacterial investigations revealed no antibodies to yersinia, mumps or toxoplasma virus. Paul-Bunnell and tests for hepatitis-associated antigen and antistreptolysin were negative. Several cultures from feces and duodenal material grew Coxsackie virus B5. Neutralizing antibody titer against the virus showed more than a 4-fold increase. A 38-year-old man with jaundice was admitted to the hospital and 7 days later developed a typical picture of acute pancreatitis. Isolation of virus from feces yielded Coxsackie B5. Neutralizing antibodies against the virus were increased 4-fold. The role of Coxsackie viruses in clinical acute pancreatitis is obscure. Since neither patient had signs of diabetes mellitus, these observations do not support a possible association between epidemics of Coxsackie virus infection and the sudden onset of diabetes in children and young people. It is noted that the father of the 27-year-old woman died following surgery on a pancreatic abscess several weeks before the woman's admission to the hospital.

7554 PERITONEAL LAVAGE THERAPY IN HEMORRHAGIC PANCREATITIS.

(E.) Rosato, E. F.; Mullis, W. F.; Rosato, F. E. (Dept. Surg., Univ. Pennsylvania, Philadelphia). *Surgery* 74(1):106-115, 1973.

Peritoneal lavage was used to treat hemorrhagic pancreatitis in 44 dogs. The 24 hr survival rate (86 vs 33%) as well as long-term survival rate (32 vs 7%) was significantly higher in the lavage group than in the control group. Peritoneal lavage lessened the absorption of toxic products as judged by a lower serum amylase concentration (4.8×10^3 vs 7.5×10^3) and a higher serum calcium concentration (7.6 vs 5.7). Within the treated group, 3-day survivors had a significantly lower peritoneal amylase at 24 hr than did nonsurvivors. The experiments support the hypothesis that peritoneal lavage improves the survival after acute pancreatitis by removing toxic products from the peritoneal cavity, thereby preventing their systemic absorption. The application of this principle to patients is illustrated by the case reports of 6 patients (3 males and 3 females, aged 14-69 yr) treated by postoperative lavage of the lesser peritoneal sac. It is suggested that, late in the course of severe pancreatitis, operative catheter placement, as opposed to percutaneous, be used since a large proportion of patients will have necrosis of the pancreas which is not amenable to lavage alone but requires direct placement of drains in the lesser sac. Early in the course of the disease, when necrosis is not likely present, percutaneous dialysis may be used.

7555 THE ROLE OF IMMUNOLOGICAL MECHANISMS IN PANCREATIC DISEASES.

(Ger.) Velbri, S.; Nutt, H.; Kasesalu, G. (Central Lab. Sci. Med., Tartu State Univ., USSR). *Z. Gesamte Inn. Med.* 28(8):222-227, 1973.

Circulating antibodies to normal pancreatic antigen and blast transformation reactions with pancreatic antigens and insulin were investigated in 98 patients with various forms of pancreatitis, 137 patients with diabetes mellitus, and 136 controls (56 normal subjects and 80 patients with other gastrointestinal diseases). These subjects ranged in age from 3 to 78 yr. Antibodies to normal pancreatic antigen were detected in half (49) of the patients with pancreatitis but in only 9 of the 134 with diabetes. A correlation was observed between the presence of circulating antibodies and the activity of the inflammatory process as determined by the WBC, shift of the differential count to the left, increase in the erythrocyte sedimentation rate, and increased urinary diastase. Blast transformation reactions in peripheral lymphocyte cultures were investigated with pancreatic antigens prepared by alkaline extraction of defatted tissue (antigen A) and extraction of tissue with acidified alcohol (antigen B, which contains primarily material from the endocrine pancreas). Lymphocytes sensitized to pancreatic antigen A were found in 59 of the 98 patients with pancreatitis, while 29 of 76 patients had lymphocytes sensitized to antigen B. The blast transformation reaction was more common in patients with inactive pancreatitis and in those with no circulating antibodies. Lymphocytes sensitized to antigen A were somewhat more common among the 54 patients with disturbances in exocrine pancreatic function, while lymphocytes sensitized to antigen B and to insulin were more common among the 40 patients with disturbances in endocrine pancreatic function. Of 13 patients with both pancreatitis and diabetes, 8 had circulating antibodies to pancreatic antigen, 6 had lymphocytes sensitized to antigen A, 2 had lymphocytes sensitized to antigen B, and 5 had lymphocytes sensitized to insulin.

7556 EARLY RESPIRATORY INSUFFICIENCY IN ACUTE PANCREATITIS.

(E.) Ranson, J. H.; Roses, D. F.; Fink, S. D. (New York Univ. Med. Ctr., N.Y.). *Ann. Surg.* 178(1):75-79, 1973.

The incidence and prognostic significance of early respiratory insufficiency has been studied by measuring arterial blood gas within the first 48 hr after diagnosis in 40 patients (35 men and 5 women, aged 20-92 yr) with acute pancreatitis. Pancreatitis was associated with alcoholism in 33 and with biliary disease in 4 patients. Treatment consisted of nasogastric suction, i.v. fluids, and antibiotics in all cases. Arterial P_{O2} fell below 75 mm Hg in 23 patients (58%). In this group, mean low arterial P_{O2} was 63.1 mm Hg, mean arterial pH was 7.48, and P_{CO2} 30.2 mm Hg. At this time clinical or radiographic evidence of pulmonary complications were found in only 3 patients. There was a tendency for the degre of early hypoxia to be related to the severity of th

ancreatitis, but marked hypoxia occurred in some pa-
ients with mild pancreatitis. Early hypoxia did not
orrelate with serum amylase, serum Ca^{++}, volume of
.v. fluids administered, or overall mortality. Even-
ual operation (34.8%) and late pulmonary complications
38%) were more frequent after early hypoxia. The
ccurrence of early respiratory insufficiency has no
efinite prognostic significance as to the course of
he pancreatitis. The late course of respiratory
nsufficiency appears related to that of the under-
ying pancreatitis.

557 FIBRINOGEN AND ALBUMIN CATABOLISM IN EXPERIMENTAL PANCREATITIS IN THE RAT.
.) Wardle, E. N. (Royal Victoria Infirm., New-
astle upon Tyne, England). *J. Surg. Res.* 15(2):
2-131, 1973.

brinogen and albumin catabolism were investigated
hooded rats before and after induction of pan-
eatitis by using ^{125}I-labeled rat fibrinogen and
^{31}I-labeled albumin. Shwartzman reactions were
oduced within the pancreas by injecting trypsin,
rpentine, 50% glycerol, olive oil, *Escherichia*
li endotoxin (100 µg), or staphylococcal α-hemolysin
00 µg) backwards through the common bile duct. Rats
ven bacterial endotoxin or toxin also received
0 µg/100 g i.v. 24 hr later. Some glycerol-treated
ts were also injected with neodymium-3-isonicotinate
ich is known to enhance intravascular coagulation.
e common bile duct was not ligated in any of these
ts. Histological studies revealed that olive oil
oduced the greatest pancreatic damage: difuse
terstitial pancreatitis with fat necrosis. The
ilure to induce hemorrhagic pancreatitis by any of
ese methods may be due to the diffuse nature of the
atomy, i.e., the rat has no main pancreatic duct but
number of ductules drain from the lobular mesenteric
ncreas into the common bile duct. Histological
idies showed that fibrin thrombi were present in
lungs of some rats, while tracer and immunofluor-
ence techniques revealed that fibrin was presen
both the lungs and kidneys. Fibrin deposition
s accentuated in animals given neodymium-3-
nicotinate. Fibrinogen catabolism increased
gnificantly in all groups except those given
ycerol; this is a manifestation of the profound
sturbance in protein metabolism in pancreatitis.
marked increase in fibrinogen catabolism occurred
glycerol-treated animals when neodymium-3-
nicotinate was administered. Injection of olive
l caused only a transient increase in albumin
abolism. Contrary to findings reported for dog
man, an increase occurred in fibrinolysis, sug-
ting that it would be unlikely for fibrin thrombi
pass through the pulmonary circulation into the
neys. Therefore, fibrinogen catabolism in the
is probably secondary to intravascular coagula-
n, particularly in the pancreas itself. Evidence
found that the following factors contribute to
shock of pancreatitis: hypovolemia and hemocon-
tration, hemoglobinemia, intravascular coagulation,
uced osmotic pressure of the blood due to increased
s of albumin into the damaged pancreas, and acti-
ion of the kallikrein and fibrinolytic systems.
is recommended that the use of Trasylol, an inhibitor of fibrinolysis and kallikrein be avoided in the treatment of pancreatitis.

7558 CHRONIC PANCREATITIS. *(Fr.)* Sarles, H.; Sahel, J. (St. Marguerite Hosp., Marseille, France). *Acta Gastroenterol. Belg.* 36(3):173-199, 1973.

7559 ALTERATIONS OF LIVER METABOLISM ASSOCIATED WITH EXPERIMENTAL ACUTE PANCREATITIS. *(E.)* Kitamura, O.; Ozawa, K.; Honjo, I. (Kyoto Univ. Fac. Med., Japan). *Am. J. Surg.* 126(3):379-382, 1973.

7560 DISTANT DISSECTION OF A PANCREATIC PSEUDOCYST INTO THE RIGHT GROIN. *(E.)* Salvo, A. F.; Nematolahi, H. (Maine Med. Ctr., Portland). *Am. J. Surg.* 126(3):430-432, 1973.

7561 CANALICULAR CELLS AND ONCOCYTES IN THE HUMAN PANCREAS. A COMPARATIVE STUDY OF THE NORMAL STATE WITH CHRONIC PANCREATITIS. *(Fr.)* Tasso, F.; Sarles, H. (Res. Unit Pathol. Dig., Marseille, France). *Ann. Anat. Pathol. (Paris)* 18(3):277-300, 1973.

7562 OSTEO-ARTICULAR COMPLICATIONS IN TWO CASES OF CHRONIC CALCIFYING PANCREATITIS TREATMENT BY WIRSUNGO-JEJUNOSTOMY. *(Fr.)* Sarles, H.; Capitaine, Y. (Digest. Pathol. Res. Unit, I.N.S.E.R.M., Marseille, France). *Arch. Fr. Mal. App. Dig.* 62(1):61-65, 1973.

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7564 AZATHIOPRINE-INDUCED ACUTE PANCREATITIS. *(E.)* Kawanishi, H.; Rudolph, E.; Bull, F. E. (Univ. Michigan Med. Ctr., Ann Arbor). *N. Engl. J. Med.* 289(7):357, 1973.

7565 PANCREATIC DISEASE WHICH WAS NOT CLINICALLY DIAGNOSED IN A SERIES OF PATIENTS WITH CHOLELITHIASIS. *(Sp.)* Obregon Icaza, J. L.; Sabas Olabarria, J. A.; Idiondo Arteche, V.; Sarabia Garcia, S. (Generalisimo Franco Munic. Hosp., Bilbao, Spain). *Rev. Esp. Enferm. Apar. Dig.* 39:547-556, 1973.

7566 THE PLACE OF SURGERY IN THE PRESENT TREATMENT OF ACUTE PANCREATITIS. *(Fr.)* Guivarc'h, M. (Surg. Hosp., Paris, France). *Concours Med.* 95(21):3835-3849, 1973.

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7571 CLINICAL AND RADIOLOGICAL FINDINGS IN CHRONIC CALCAREOUS PANCREATITIS. *(Ger.)* Fumagalli, I.; Hammer, B.; Wirth, W.; Ammann, R. (Dept. Intern. Med., Univ. Zurich, Switzerland). *Schweiz, Med. Wochenschr.* 102(37):1316-1318, 1972.

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7573 OBJECTIVES AND RESULTS OF SURGERY FOR CHRONIC AND RECURRENT PANCREATITIS. *(Fr.)* Mallet-Guy, P. (no affil.). *Union Med. Can.* 102(9):1916-1920, 1973.

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7575 HEREDITARY PANCREATITIS IN A NEWCASTLE FAMILY. *(E.)* Sibert, J. R. (Newcastle Gen. Hosp., Newcastle upon Tyne, England). *Arch. Dis. Child.* 48(8):618-621, 1973.

7576 TEN CASES OF CHRONIC PANCREATITIS. *(Sp.)* Lopez Zaborras, J.; Castillo Bernal, E. (no affil.). *Rev. Esp. Enferm. Apar. Dig.* 39(6):709-722, 1973.

7577 STATE OF THE BILIARY TRACT IN PATIENTS WITH CHRONIC PANCREATITIS. *(Rus.)* Lukash, L. K. (Inst. Nutr., Moscow, USSR). *Kazan. Med. Zh.* (3):18-20, 1973.

7578 CHRONIC PANCREATITIS WITH CIRCUMSCRIBED SUPPURATION MANIFESTED BY DUODENAL STENOSIS. *(Fr.)* Vayre, P.; Delavierre, P.; Debbasch, L.; Causse, P.; Bourdais, J. P. (Vaugirard Hosp., Paris, France). *Sem. Hop. Paris* 49(28):2091-2093, 1973.

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(E.) Daum, F.; Rosen, J. F.; Boley, S. J. (Montefiore Hosp., Bronx, N.Y.). *J. Pediatr.* 289(11):586-1973.

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7600 A CASE OF PRIMARY HYPERCHYLOMICRONAEMIA. *(It.)* Giardini, O.; Scalercio, A.; Anibaldi, A.; Castro, M. (1st Pediatr. Clin., Univ. Rome, Italy). *Minerva Pediatr.* 25(11):506-511, 1973.

7601 ACUTE PANCREATITIS WITH EXTENSIVE PERIPHERAL FAT NECROSIS SIMULATING ERYTHEMA NODOSUM AND AN ABDOMINAL CYST. *(E.)* Dobbins, III. W. O.; Liberman, M. S. (George Washington Univ. Med. Ctr., Washington, D.C.). *Med. Ann. D.C.* 42(7):319-322, 1973.

See also, 6210, 6753, 6798, 6835, 6948, 7159, 7224, 7292, 7520, 7524, 7761.

7602 EFFECT OF EXTRACORPOREAL LIVER PERFUSION ON THE ELECTROENCEPHALOGRAM OF PATIENTS IN COMA DUE TO ACUTE LIVER FAILURE.

(E.) Kennedy, J.; Parbhoo, S. P.; MacGillivray, B.; Sherlock, S. (Roy. Free Hosp., London, England). *Q. J. Med.* 42(167):549-561, 1973.

Clinical findings and changes in the electroencephalogram (EEG) are described for 5 patients (3 women and 2 men, aged 22-50 yr) treated for hepatic coma by extracorporeal pig-liver perfusion. All patients had been in deep comas due to acute liver failure for 31 to more than 64 hr prior to perfusion and had not responded to at least 24 hr of conventional therapy. Liver failure was caused by viral hepatitis (3 cases), acute fatty liver of pregnancy (1 case), and ingestion of 30-55 g acetaminophen (1 case). In 4 cases the EEG tracings were characterized by decreased amplitude associated with a low frequency, blunting of triphasic waves where initially present, and periods of flattening; 1 patient had no cerebral activity. After perfusion, 2 patients including the one who initially had no cerebral activity, fully regained consciousness and have survived 24 and 30 months, resp. Dramatic improvement occurred in the clinical condition and EEG of these patients after perfusion, but a full return to normal did not occur for 4 weeks although they were conscious within 48 hr. Clinical improvement occurred in 2 more patients, but the EEG remained featureless and of low amplitude; both patients died. The remaining patient died shortly after perfusion before another EEG could be recorded. A good correlation was obtained between cerebral metabolism (cerebral blood flow, cerebral oxygen, and glucose consumption and oxygen glucose index) and the EEG and clinical state. It is recommended that EEG monitoring be included in routine management of patients with acute liver failure.

7603 THE EFFECT OF VENESECTION THERAPY ON LIVER TISSUE IN PORPHYRIA CUTANEA TARDA.

(E.) Chlumsky, J.; Malina, L.; Chlumska, A. (Med. Fac., Charles Univ., Prague, Czechoslovakia). *Acta Hepatogastroenterol.* 20(2):124-130, 1973.

Liver biopsies were examined in 43 patients (40 men and 3 women, aged 29-69 yr) with porphyria cutanea tarda. Biopsies were also examined after venesection therapy administered 2-7 times in 21 of these patients. Clinical diagnosis was confirmed by coproporphyrin excretions of 173-2000 µg/day and uroporphyrin excretions of 2400-9500 µg/day. All but 4 patients had clinically manifest disease. Histories were obtained of the following possible etiological factors: viral hepatitis (11 cases), alcohol consumption (18), tuberculosis (7), syphilis (6), diabetes mellitus (6), peptic ulcer (4), gallbladder disease (11), starvation (3), and lead exposure (1). Noncharacteristic findings were present in liver biopsies from 7 patients (16.3%); these included large-droplet steatosis and hemosiderosis. Fibrosis was present in 20 cases (46.5%) and chronic hepatitis in 16 (37.2%); none of the patients had cirrhosis. The severity of changes in the liver appeared to be related to the patient's age rather than to the duration of the porphyria. After venesection therapy performed on 21 patients there was remission of steatosis in 8 cases and of hemosiderosis in 4. One patient with fibrosis developed chronic hepatitis, while 3 patients with chronic hepatitis improved and fibrotic changes were observed. Skin changes regressed and uroporphyrin excretion normalized, but clinical findings remained unchanged.

7604 AN UNUSUAL COMPLICATION FOLLOWING LOCAL ANESTHESIA FOR LIVER BIOPSY. *(E.)*

Dobronte, Z.; Varro, V. (Univ. Med. Sch., Szeged, Hungary). *Endoscopy* 4(3):170-172, 1972.

A 40-yr-old male was admitted for hepatosplenomegaly of unknown etiology. Diagnostic tests indicated thrombosis of the portal vein. Total serum bilirubin, serum alkaline phosphatases, and SGOT values were elevated. X-ray examination revealed esophageal varices. In preparation for liver biopsy, 6 days after an uncomplicated laparoscopy, the intervening tissues in the intercostal space as deep as the surface of the liver were anesthetized with a thin needle using 1% lidocaine solution. As the liver capsule was reached, violent pain was experienced in the right hypochondrium, spreading into the right shoulder. Biopsy was not completed. About 48 hr later, the patient's condition deteriorated, abdominal pain increased and became diffuse, and signs of subileus gradually developed. Peristaltic sounds were less frequent but audible. As no clinical evidence of peritonitis was found and conservative therapy caused some improvement, no exploration was made. On the 4th day ascites was proven and surgery performed. The bilious fluid was sterile. On the upper lateral surface of the liver, probably at the site of the puncture, bile was slowly oozing from a minimal injury. The patient died with symptoms of circulatory failure and autopsy revealed a congenital liver anomaly consisting of a cavernoma-like transformation and extensive thrombosis of the portal vein, leading to marked fibrosis of the multilobular liver. Around the injury from the fine needle, a number of fibrotic bundles contained a number of unusually wide bile ducts of different diameters. The injury of one of these ducts near the surface produced diffuse biliary peritonitis. Immediate surgery is recommended at even the slightest hint of bile oozing after liver biopsy.

7605 CLONORCHIASIS STUDIED BY PERCUTANEOUS CHOLANGIOGRAPHY, AND A THERAPEUTIC TRIAL OF TOLUENE-2,4-DIISOTHIOCYANATE. A CASE REPORT.

(E.) Okuda, K.; Emura, T.; Morokuma, K.; Kojima, S.; Yokagawa, M. (Chiba Univ. Sch. Med., Japan). *Gastroenterology* 65(3):457-461, 1973.

A 38-yr-old farmer who had begun eating raw carp several months before presented with hepatomegaly, increased serum alkaline phosphatase, and eosinophilia. Hepatomegaly regressed and alkaline phosphatase levels decreased without treatment, while moderate increases occurred in SGOT and SGPT. A duodenal aspirate contained many *Clonorchis sinensis* ova, and liver biopsy suggested chronic inflammation of the biliary tract. Percutaneous transhepatic cholangiography disclosed many small filling defects in moderately dilated intrahepatic bile ducts which had a hazy appearance, probably because of mucous exudate. Several small particles were present in the gallbladder, the mucosa of which had a mosaic or honeycomb appearance. Conventional therapy with chloroquine (0.6 g/day p.o. for 36 days) and antimony sodium tartrate (20 ml of a 3% solution i.v. every other day for 30 days) failed to expel the flukes. Even direct injection of antimony sodium tartrate (20 ml of a 3% solution) directly into the bile duct failed to decrease the fecal egg count. Two courses of 1,4-bis(trichloromethyl) benzene (30 mg/kg/day p.o.) and toluene-2,4-diisothiocyanate (1.0 mg/kg/day p.o.) for 5 consecutive days each did eliminate ova from the stools. No side effects occurred except for a transient increase in serum transaminases and alkaline phosphatase immediately after therapy. This is the first trial of toluene-2,4-diisothiocyanate in man.

7606 WILSON'S DISEASE OR CHRONIC COPPER POISONING? *(E.)* Walker-Smith, J.; Blomfield, J. (Roy. Alexandra Hosp. Children, Camperdown, Australia). *Arch. Dis. Child.* 48(6):476-479, 1973.

A 14-month-old boy with progressive abdominal swelling had ascites and a small cirrhotic liver at laparotomy. SGOT, SGPT, and serum alkaline phosphatase activities were increased while total serum protein, albumin, and the prothrombin index were decreased; generalized aminoaciduria was detected but serum amino acid levels were normal. Liver biopsy showed severe micronodular cirrhosis and markedly increased copper contents in the nodules. Plasma free copper and urinary copper levels were increased, while plasma ceruloplasmin levels were decreased. Although no Kaiser-Fleisher rings were observed, these results suggested that the boy had Wilson's disease. However, since it is unusual for Wilson's disease to occur with such severe manifestations in a patient so young, the possibility of chronic copper poisoning was investigated. The family who had moved to a dairy farm 5 months before patient's birth obtained their water from a well through copper pipes. The pH of the water was 4.4, and after passage through the copper pipes had a copper concentration of 675 μg/100 ml. Investigation of other members of the family showed no clinical evidence of copper poisoning, and their plasma copper levels, serum transaminases, and urinary copper levels both before and after penicillamine were normal except in the mother who had urinary copper values in the upper normal range; these were consistent with values found in heterozygotes of Wilson's disease. Treatment with penicillamine was unsuccessful and the child died 6 weeks after hospitalization. At autopsy very high copper were found in the boy's liver, kidney, and heart, but brain copper levels tended to be lower than in other cases of Wilson's disease. The diagnosis in this case is uncertain. The boy may have had Wilson's disease and, because of his exposure to high copper levels, developed clinical manifestations at an earlier age than usual. It is also possible that he died of chronic copper poisoning. The third possibility is that he had an intrauterine or neonatal liver infection and was subsequently exposed to high copper levels. It is recommended that all patients suspected of having Wilson's disease have the copper content of their drinking determined so that the role of excess dietary copper intake in the pathogenesis of liver disease will be more clearly understood.

7607 HEPATIC ALTERATIONS IN HODGKIN'S DISEASE. *(E.)* Davey, F. R.; Doyle, W. F. (Letterman Gen. Hosp., San Francisco, Calif.). *N.Y. State J. Med.* 73(15):1981-1986, 1973.

A clinicopathologic analysis of livers in 78 patients with Hodgkin's disease revealed intrahepatic Hodgkin's disease in 41 (70%) of the 59 studied at autopsy and in 4 (12%) of liver biopsies. Hodgkin's disease infiltrates were found more frequently in the spleen, periaortic lymph nodes, hepatic portal, and other retroperitoneal lymph nodes, and in bone marrow in Hodgkin's disease-involved livers than in uninvolved livers. Massive hepatic Hodgkin's disease infiltrates were frequently associated with abnormal liver function tests, jaundice, and hepatomegaly, while normal liver function tests were often associated with microscopic or small infiltrates in the liver. Hodgkin's disease was found predominantly in portal areas, especially when the lesion was microscopic. Terminally, the infiltrates were associated with marked portal fibrosis and focal necrosis. In 9 of the cases studied at autopsy (23%), invasion of intrahepatic portal veins had occurred. Tissue sections revealed sarcoid-like granulomas in 5 (15%) and nonspecific portal inflammation in 8 (24%) of biopsied cases. Microscopic examination of the liver remains the best method to identify intrahepatic Hodgkin's disease since it may be the only diagnostic procedure to unequivocally demonstrate liver dysfunction in patients with Hodgkin's disease.

7608 NEONATAL CHOLESTASIS IN ALPHA-1-ANTITRYPSIN DEFICIENT CHILDREN. *(E.)* Aagenaes, O.; Matlary, A.; Elgjo, K.; Munthe, E.; Fagerhol, M. (Univ. Hosp., Oslo, Norway). *Acta Paediatr. Scand.* 61(6):632-642, 1972.

Clinical, histological, and immunohistochemical examinations were performed on 5 children with liver disease who were homozygotes for the α_1-antitrypsin deficiency gene Pi^{Z}, 2 adult homozygotes without liver disease, 3 monozygotes (1 child and 2 adults), and control children with intra- and extrahepatic cholestasis. The clinical picture of liver disease associated with Pi^{Z} homozygosity in infancy was a neonatal cholestasis. α_1-Antitrypsin accumulated in the liver cells in amounts which were related to the genotype (the largest amounts in homozygotes and smaller amounts in monozygotes) and were independent of the severity of liver disease. All 5 children had inherited one Pi^Z gene from each parent. It is concluded that α_1-antitrypsin deficiency is caused by a mutation at the locus for α_1-antitrypsin structural genes, resulting in abnormal protein which is released from liver cells at a markedly reduced rate. Tissue damage may result from nonspecific interference of accumulated protein with vital intracellular processes or by excessive specific inhibition of important proteolytic enzymes in the liver cells. If the liver disease does result from protein accumulation, treatment must employ methods to stimulate release of material from the endoplasmic reticulum.

7609 HEPATIC BLOOD FLOW AND SURGERY OF PORTAL HYPERTENSION. PRELIMINARY RESULTS. *(E.)*

Laudanna, A. A., Strauss, E.; Nunes, J. E. O.; Silva, L. C.; Raia, S.; Okumura, M.; Kieffer, J. (Univ. Sao Paulo, Sch. Med., Brazil). *Acta Hepatogastroenterol.* 20(2):134-137, 1973.

Hepatic blood flow was measured by ^{198}Au in 15 patients (8 males and 7 females, aged 6-59 yr) before and after several different shunting procedures for portal hypertension correction. Diagnoses in these 15 cases included schistosomiasis mansoni in 13 and cirrhosis in 2. The surgical procedures included conventional splenorenal anastomosis (5), side-to-side splenorenal anastomosis (2), distal splenorenal anastomosis (4), portocaval anastomosis (1), splenectomy with azygos-portal circulation decompression (3). Preliminary results suggest that hepatic blood flow could be successfully used to evaluate the final results of surgical correction of portal hypertension. Protocaval anastomosis, conventional and side-to-side splenorenal anastomosis were followed by reduced hypertension. Distal splenorenal anastomosis and splenectomy with azygos-portal circulation decompression were usually followed by increased liver perfusion.

7610 BUDD-CHIARI SYNDROME IN A PATIENT WITH PAROXYSMAL NOCTURNAL HEMOGLOBINURIA. *(E.)*

Falchuk, Z. M.; Leventhal, B. G. (Peter Bent Brigham Hosp., Boston, Mass.). *Am. J. Dig. Dis.* 18(10):900-904, 1973.

A 29-yr-old white male presented with anemia of unknown origin. Steroid therapy was instituted. Splenectomy performed 1 yr later still did not arrest the anemia. Paroxysmal nocturnal hemoglobinuria was diagnosed the following year. After 5 years, he presented with bilateral lower quadrant discomfort. The abdomen was diffusely tender and ascites was suspected. The liver edge was hard, mildly tender, and not pulsatile. Alkaline phosphatase was 174 IU; bilirubin, 0.6 mg/100 ml; and SGOT, 58 IU. Percutaneous aspiration of the abdomen produced ascitic fluid. After 3 weeks, a hepatic venogram was performed, because of persisting symptoms and increasing ascites. Only the right hepatic vein could be entered after some difficulty. A radiopaque thrombus in the lumen of the vessel prevented easy passage of the catheter. The dye escaped beyond the thrombus. An abnormal vascular pattern was observed, consisting of a network of short, fine tortuous vessels. Warfarin therapy was started but discontinued 3 weeks later due to significant hematuria. Spironolactone and thiazide therapy was initiated. The patient was discharged in stable condition. Spironolactone was discontinued after 15 months due to gynecomastia. This patient is the 5th reported case of proven hepatic vein thrombosis and Budd-Chiari syndrome in a patient with paroxysmal nocturnal hemoglobinuria and is the first to survive more than 3 yr after onset of symptoms.

7611 CHOLEDOCHAL CYST: A CONCEPT OF ETIOLOGY.

(E.) Babbitt, D. P.; Starshak, R. J.; Clemett, A. R. (Milwaukee Children's Hosp., Wis.). *Am. J. Roentgenol. Radium Ther. Nucl. Med.* 119(1): 57-62, 1973.

An anomalous arrangement of the pancreaticobiliary ductal system has been found in 7 cases of choledochal cyst. It is suggested that this anomaly precludes the development of a sphincter at the junction of the pancreatic and common bile ducts. The pressure difference between the common duct and the pancreatic duct allows pancreatic juice to flow into the bile ducts if the sphincter is not present, causing recurrent bouts of cholangitis that result in thickening of the wall of the common duct. As further dilation of the common duct occurs, it expands anteriorly and becomes obstructed at the distal end of the cyst from edema or eventually, fibrosis. It is suggested that decompression of the cyst is all that may be undertaken in acutely ill patients, with abnormalities to be corrected at a later time. Division of the cyst at the distal end would be performed to terminate the communication responsible for allowing pancreatic juice to enter biliary ducts. Direct anastomosis of the remaining portion of the cyst to the duodenum or jejunum, or to a Roux-en-Y anastomosis should then be performed. Cholangiographic demonstration of the pancreaticobiliary junction is necessary prior to such surgery.

7612 UNILOBAR VENO-OCCLUSIVE DISEASE OF THE LIV ANGIOGRAPHIC DEMONSTRATION OF INTRAHEPATIC COMPETITION SIMULATING HEPATOMA. *(E.)*

Galloway, S. Casarella, W. J.; Price, J. B. (Columbia-Presbyterian Med. Ctr., New York, N.Y.). *Am. J. Roentgenol. Radium Ther. Nucl. Med.* 119(1):89-94, 1973

A 55-yr-old female presented for evaluation of polycythemia and ascites. An adenoma of the thyroid gland had been removed 14 months earlier, 6 months after which she complained of headaches and dizziness which was diagnosed as polycythemia. Anticoagulant therapy appeared helpful, but 9 months later after the drugs had been discontinued, the fatigue and dizziness returned. A phlebotomy was performed, shortly after which her legs and abdomen swelled.

Thiazide diuretics offered no relief. Total bilirubin was 1.8 mg%; alkaline phosphatase, 250 U; and SGOT, 222 U. Visceral angiography revealed a hypervascular, shrunken right lobe of the liver with markedly tortuous arteries and suggested neovascularity. The left lobe was enlarged with stretching and draping of the arteries. The right portal vein had a discrete cut-off typical of an anatomic obstruction. This case showed intrahepatic competition between the right lobe with its occluded hepatic veins and functionally occluded portal veins and the left lobe with its more normal portal blood supply and hepatic venous drainage. The roentgenographic appearance superficially mimicked a hepatoma. Angiographically the shrunken right lobe closely simulated cirrhotic features. The only truly diagnostic technique is injection of contrast material directly into the hepatic parenchyma which, in this case, confirmed the functional nature of the apparent right portal vein occlusion and established the hepatic hemodynamics that are diagnostic of hepatic vein thrombosis.

7613 CHOLESTATIC JAUNDICE IN THE COURSE OF GENERALIZED AMYLOIDOSIS WITH INVASION OF THE IVER ASSOCIATED WITH ATYPICAL MYELOMA. *(Fr.)* Touche, .; Gouin, B.; Prell, J. L.; Blanc, D.; Teillet, F.; arge, J.; Hardouin, J. P. (Corvisart Hosp., Charleille-Mezieres, France). *Ann. Med. Interne (Paris)* 24(4):303-308, 1973.

he seventh case of amyloidosis presenting as choestatic jaundice is reported. A 52-yr-old man with 5-month history of diarrhea, steatorrhea, and abominal pain was hospitalized with hepatomegaly and scites, whereupon he developed jaundice. Increases ccurred in total bilirubin, total cholesterol, alkaine phosphatase, SGOT, and SGPT. Immunoelectrohoresis revealed a pathological κ-type of immunolobulin, characteristic of myeloma, with a decrease n other immunoglobulin fractions. The patient died n hepatic coma. Although no bone lesions were deected radiologically, the patient did not complain f ostealgia, and localized plasma cell tumors were ot present at autopsy, a diagnosis of myeloma was stablished because of diffuse infiltrates of lymphoytes and plasma cells present in the bones at autop-. Other findings included purpuric lesions of e gastric mucosa and amyloid deposits in the liver, leen, intestine, thyroid, pancreas, adrenals, heart, ngs, and kidneys. No evidence of extrahepatic liary obstruction was found. Since it has been ported that reticuloendothelial macrophages absorb ght-chain immunoglobulins, break them down in the sosomes by proteolysis, and synthesize amyloid terial, it is suggested that amyloidosis is an omaly involving an immunoglobulin which may be oduced in excess by plasma cell proliferation ocrring in the course of various diseases or maligncies.

14 DETECTION OF SERUM ALPHA FETOPROTEIN IN CLINICAL DIAGNOSIS AND IN MASS SURVEY OF IMARY LIVER CANCER. *(E.)* Anonymous. (Shanghai Co-ordinating Group Prevention Treatment Cancer, China). *Chinese Med. J.* (8):98-99, 1973.

The Ouchterlony double diffusion method and countercurrent electrophoresis were used to identify serum α-fetoprotein in 4621 serum samples. The latter method proved 10-15 times more sensitive than the former. By using the immunodiffusion method, as little as 500 m μg/ml α-fetoprotein could be detected. The 4621 samples were obtained from 797 patients with primary hepatocellular carcinoma, 6 with cholangiocellular carcinoma, 52 with metastatic liver cancer, 147 with extrahepatic neoplasma, 2342 with non-neoplastic liver and biliary diseases, and 482 with other nongastrointestinal diseases; 791 healty donors served as controls. Of those with primary hepatocellular carcinoma, 75.5% had positive α-fetoprotein tests. In a further study of 66,378 persons, 151 were positive for α-fetoprotein and of these, 131 cases were clinically or pathologically confirmed as primary liver cancer. From these studies it is apparent that primary hepatocellular cancer may be diagnosed before clinical symptoms appear by a positive α-fetoprotein test. The average content of α-fetoprotein (8.3 mg/100 ml) was lower in positive sera obtained from mass screening of the public than it was (21.9 mg/100 ml) in positive sera obtained from patients with chronic liver disease.

7615 THE SURFICAL MANAGEMENT OF PRIMARY HEPATOCELLULAR CARCINOMA IN UGANDA. *(E.)* Harrison, N. W.; Dhru, D.; Primack, A.; Bhana, D.; Kyalwazi, S. K. (Uganda Cancer Inst., Kampala). *Br. J. Surg.* 60(7):565-569, 1973.

Hepatocellular carcinoma is a common tumor in Uganda. Of 120 patients with hepatoma admitted in a 2 1/2 yr period, 36 (28%) underwent surgery. Major hepatic resections were performed on 10 patients, and a hepatic artery catheter was used for regional infusion of dichloromethotrexate (10 mg/m^2 for 7-10 days). An additional 7 patients received systemic chemotherapy with N(3,5-dichloro-4(2,4)diamino-6-pteridinyl(methyl[methylamino}benzol]glutamic acid, 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea, or a combination of 1.3-bis-(2-chloroethyl)-1-nitrosourea and 5-fluorouracil; 7 patients were not treated. Survival times were longer in patients treated surgically or with regional infusion of dichloromethotrexate than in those receiving systematic chemotherapy or no treatment. Although hepatic resection appears to be the best method for treating hepatocellular carcinoma, only a small fraction of the patients had operable tumors. The mortality in operated patients was 30%. Complications included subphrenic abscess in 2 cases. Three of these 10 patients are still alive, but only 1 appears to be tumor-free.

7616 EXTRACORPOREAL CIRCULATION IN HYPOTHERMIA AS USED FOR TOTAL-BODY WASHOUT IN STAGE IV HEPATIC COMA. *(E.)* Cline, R. E.; Klebanoff, G.;

Armstrong, R. G.; Stanford, W. (Wilford Hall USAF Med. Ctr., Lackland, Tex.). *Ann. Thorac. Surg.* 16(1):44-51, 1973.

The rapid infusion of a refrigerated, buffered albumin electrolyte solution combined with simultaneous exsanguination (total-body washout) was used to treat 19 patients; 14 had either acute viral hepatitis or Reyes' syndrome and the other 5 had cirrhosis or chronic liver disease. Of the 14, there are 6 long-term survivors. None of the 5 with cirrhosis or chronic liver disease survived more than a few days after total-body washout. The sensorium began to clear about 24 hr after the procedure. In long-term survivors, the liver function test values gradually returned to normal levels after rising to abnormal levels almost immediately after the procedure was completed. Transient hyperfibrinolysinemia usually developed in the first 2 hr, but spontaneously reversed in 4 hr. A brisk and beneficial diuresis usually followed the procedure during the first 24 hr. This safe, simple procedure also promptly controls bleeding problems, and helps to stabilize blood pressure. No serious complications occurred, and the procedure now seems indicated when conventional forms of therapy fail to control progressive hepatic coma.

7617 CIRCULATING CONVERSION PRODUCTS OF C3 IN LIVER DISEASE. EVIDENCE FOR IN VIVO ACTIVATION OF THE COMPLEMENT SYSTEM. *(E.)* Teisberg, P.; Gjone, E. (Univ. Hosp., Oslo, Norway). *Clin. Exp. Immunol.* 14(4):509-514, 1973.

Circulating conversion products of the third components of human complement (C3) were sought for in different forms of liver disease by the method of antigen-antibody crossed electrophoresis. Immunochemical determinations of C3 and C4 by the single radial immunodiffusion method were performed simultaneously. The conversion product C3b was found in 4 of 12 patients with chronic active hepatitis and in 7 of 9 with primary biliary cirrhosis. It was also seen in a patient with the special form of acute hepatitis charecterized by arthritic prodromas and a high titer of hepatitis-associated antigen in serum in the acute phase. The group of chronic acute hepatitis patients had low serum C3 and C4 regardless of whether C3 breakdown products could be demonstrated. In primary biliary cirrhosis, serum levels of C3 and C4 were generally normal. It is concluded that in chronic acute hepatitis patients and in a majority of the primary biliary cirrhosis patients, activation of complement takes place *in vivo*, possibly on immune complexes deposted in the parenchymal cells. The serum level of C3 is not a good parameter of immunologic activity in liver disease.

7618 HEPATIC VEIN THROMBOSIS IN CHILDREN IN THE NEAR EAST. *(E.)* Hershko, C. (Univ. Washington Sch. Med., Seattle). *Med. Chir. Dig.* 1(1):37-40, 1972.

Reports from Egypt, Iraq, and Israel suggest that hepatic vein thrombosis may be endemic among Near Eastern children aged 1-12 yr. The onset of the disease is acute, with colicky pains and rapid ascites. There is an important collateral circulation over the abdominal wall. Hepatic function is fairly well preserved. Necropsy revealed thrombotic occlusion of the ostia of the hepatic veins with or without thrombosis of the inferios vena cava. This involvement of the large hepatic veins and the rapid onset of the disease distinguish it from the veno-occlusive disease of Jamaican children. The possibility of a congenital abnormality as an etiologic factor is excluded. It is suggested that accidental contamination of food by pyrrolizidine alkaloids or aflatoxins may be the cause. Herbal medicines are also a possible source of natural toxins. Treatment is largely symptomatic. However, heparin may be of use and a therapeutic trial of the drug is suggested at the acute initial phase of the disease or when signs of an active thrombotic process are present.

7619 RESUSCITATION OF A PATIENT IN STAGE IV HEPATIC COMA USING TOTAL BODY WASHOUT. *(E.)* Klebanoff, G.; Armstrong, R. G.; Cline, R. E.; Powell, J. R.; Bedingfield, J. R. (Wilford Hall USAF Med. Ctr., Lackland Air Force Base, Texas). *J. Surg. Res.* 13(4):159-165, 1973.

A 20-yr-old white male was initially admitted with polyarthralgia and malaise. Mild hepatic tenderness and hepatomegaly were noted. After 3 weeks time, SGOT was 4800; SGPT, 3600; total bilirubin, 10.7 mg/100 ml. The patient deteriorated and was in hepatic failure of undetermined etiology in Stage IV coma when L-dopa (50 mg/kg) was added to the prednisolone (60 mg) he was already receiving. After 2 trials with L-dopa with no result, total body washout was begun. The patient's blood volume was replaced postwashout with 4 liters whole blood and 2 liters packed cells. The whole blood was heparinized and the cells were suspended in citrate-phosphate-dextrose. It is stressed that the cooling must be maintained as near 5 C as possible. At 10 hr postoperation, the patient was in Stage II coma and improving noticeably each hour. Due to still elevated blood ammonia and the opinion that an underlying neuroconductive effect existed, a third trial with L-dopa (30 mg/kg, via nasogastric tube) was undertaken. The patient was sitting up in bed at 20 hr postoperation and has continued to improve. It is suggested that total body perfusion be used when a patient, adequately cared for with bowel sterilization, sorbitol, and protein restriction, in Stage IV coma fails to respond to L-dopa (50 mg/kg). The procedure is safer, easier, and more physiologic than any other experimental method currently available.

7620 PRIMARY LIVER TUMORS IN CHILDREN. *(Ger.)* Stauffer, U. G.; Rickham, P. P.; Gindrat, A. (Pediatr. Clin., Univ. Zurich, Switzerland). *Helv. Paediatr. Acta* 28(3):239-248, 1973.

In a 15-yr-period primary liver tumors were diagnosed in 14 children (7 girls and 7 boys, aged 3 days to 8 yr); 9 were less than 1 yr old. In addition, 2 sisters, aged 26 and 23 yr, resp., are included; both had type I glycogen storage disease. Ten tumors were malignant (5 malignant hepatomas, 2 malignant mesenchymomas, 1 hepatoblastoma, 1 hemangioendothelioma, and 1 lymphosarcoma) and 6 were benign (1 glycogen storage hepatoma, 1 hemolymphangioma, 3 hemangiomas, and 1 hepatic cyst). At laparotomy 6 of the 10 malignant liver tumors were found to be inoperable. Cytostatic agents (vincristine, cyclophosphamide, leucocristine, chlorambucil), given to 5 patients with inoperable malignant tumors, induced temporary tumor regression in 2 cases, but all 5 children died within 6 months after surgery. An inoperable hemangioendothelioma regressed spontaneously without surgery or administration of cytostatic agents. No evidence of a recurrence was found when the patient underwent surgery for a perforated appendix 15 yr later. With the exception of giant hemangiomas, the prognosis is good for benign liver tumors. Of the 6 patients with benign tumors, 4 survived. Attempts at right hemihepatectomy failed in 2 newborns with giant hemangiomas: one died on the operating table of uncontrollable bleeding while the other died 4 days after surgery with thrombosis of the superior vena cava and massive pulmonary embolism.

7621 EXTRACORPOREAL CATION-EXCHANGE CIRCUITS IN THE TREATMENT OF HYPERAMMONAEMIA OF HEPATIC FAILURE. *(E.)* Juggi, J. S. (Dept. Physiol., Univ. Malaya, Kuala Lampur, Malaysia). *Med. J. Aust.* 60 (19):926-930, 1973.

A technique of extracorporeal circulation through cation-exchange circuits was developed and applied in 4 clinical perfusions in 3 patients (2 males and 1 female; aged 8-45 yr) in advanced stages of hepatic coma with hyperammonemia. Acute infective hepatitis was present in 2 cases; portal cirrhosis in the other. A mixture of the sodium, potassium, calcium and magnesium forms of a strong cation-exchange resin, Amberlite IR-120, with a total quantity of 750 mEq was used in the perfusion columns. This mixture was effective in correcting hyperammonemia in these patients with hepatic failure. There were no adverse effects of the perfusions and other cationic constitutents of the perfused blood were not significantly altered. Some improvement in clinical status of the patients was observed and coma was sufficiently reversed in 2 of the 3. However, this improvement was not persistent probably because of the severity of the disease in these patients. All relapsed into deep coma and died. Selection of suitable patients is emphasized. The technique is simple, easily operable, inexpensive, and can be assembled at the bedside of the patient.

7622 METABOLIC DISORDER AND ENCEPHALOPATHY: STUDIES OF PHENOLIC COMPOUNDS IN DISTURBANCES IN CONSCIOUSNESS RESULTING FROM LIVER DISEASE. *(Ger.)* Ruge, W. (Med. Coll., Hannover, Germany). *Med. Welt* 23(5):149-153, 1972.

Amino acid metabolites were determined by gas chromatography in urine and serum from 19 controls with no evidence of liver disease, 4 patients with cirrhosis, 4 with active cirrhosis, 4 with encephalopathy, 4 with coma and precoma, and 4 with coma after massive variceal bleeding. Urinary levels of p-hydroxyphenylacetic acid were significantly lower in patients with liver coma than in cirrhotics or normal controls, and urinary levels of p-hydroxyphenylacetic acid were significantly higher in patients in liver coma right after massive bleeding from esophageal varices than in all other groups. Considerable variation in the urinary levels of p-hydroxyphenylpyruvic acid was observed within each of the groups studied; this may be due to the analytical method employed. Significant increases in serum tyrosine and nonprotein nitrogen levels were found in patients with liver disease and signs of encephalopathy. Serum phenol levels were significantly increased in patients in a coma after massive variceal bleeding. It is pointed out that amino acid metabolites which increase in the urine in hepatic coma are precursors of catecholamines and are related to them structurally. An imbalance of these catecholamine analogues in the brain might account for the neurological symptoms associated with hepatic insufficiency.

7623 LIVER CHANGES IN COLITIS. *(Ger.)* Bortfeldt, K.; Wiek, K.; Pichl, H. (Rudolf Virchow Munic. Hosp., Berlin, Germany). *Med. Welt* 23(31/32): 1071-1073, 1972.

Determinations of SGOT, SGPT, serum alkaline phosphatase, and 45-min BSP retention were made on 296 patients with colitis, diagnosed by rectoscopy, of unknown etiology. These consisted of 101 patients with catarrhal colitis, 139 with mild ulcerative colitis, and 56 with severe ulcerative colitis. Patients with Crohn's disease were excluded. Only untreated patients and patients with recurrences who had not undergone treatment in the past 6 months were included. Disturbances in liver function tests were found in 127 cases: in 41.6% of those with catarrhal colitis, 42.5% of those with mild ulcerative colitis, and 48.2% of those with severe ulcerative colitis. Of these 127 patients with abnormal liver function tests, 60 had a history of liver disease. Since the remaining 67 patients (22.6%) had no history of liver disease, abnormalities in liver function can be ascribed to the colitis. Because of the relatively small number of cases, no correlations were obtained between the age of the patients and the type of colitis or liver disease. There was no significant tendency for liver abnormalities to increase with increasing age.

7624 SUCROSE FEEDING IN MAN. EFFECTS ON SUBSTRATE INCORPORATION INTO HEPATIC TRIGLYCERIDES AND PHOSPHOGLYCERIDES IN VITRO AND ON

REMOVAL OF INTRAVENOUS FAT IN PATIENTS WITH HYPERLIPOPROTEINEMIA. *(E.)* Cahlin, E.; Jonsson, J.; Persson, B.; Stakeberg, H.; Bjorntorp, P.; Gustafson, A.; Schersten, T. (Dept. Surg., Univ. Goteborg, Sweden). *Scand. J. Clin. Lab. Invest.* 32(1):21-33, 1973.

Patients (11 males and 24 females) operated on for uncomplicated gallstone disease were studied. Patients with pre-β-hyperlipoproteinemia (8) and normolipoproteinemia (11) had sucrose substituted for 800 Kcal of their daily caloric intake for 2 weeks prior to operation. A group of 16 patients served as non-sucrose-fed controls. In the normolipoproteinemic patients, sucrose feeding elevated plasma triglycerides, transiently decreased cholesterol, increased basal insulin concomitant with an increased adipose tissue lipoprotein lipase activity. Only basal insulin increased significantly in pre-β-hyperlipoproteinemia. Liver triglyceride and glycogen contents were elevated after sucrose feeding, while phosphoglyceride content was lower in pre-β-hyperlipoproteinemia than in normolipoproteinemia. After sucrose feeding a higher and similar incorporation rate of labeled precursors into hepatic triglycerides was observed in normolipoproteinemia and pre-β-hyperlipoproteinemia. The incorporation rate into choline phosphoglycerides was lower in pre-β-hyperlipoproteinemia than in patients with initially normal serum lipid values. Sucrose feeding in normolipoproteinemic gallstone patients enhanced triglyceride synthesis in the liver and also the adipose tissue lipoprotein lipase activity. In pre-β-hyperlipoproteinemia, sucrose feeding caused a reduced capacity for hepatic phosphoglyceride synthesis. These findings indicate that patients with initial hypertriglyceridemia differ in their response to sucrose feeding by having a reduced capacity for hepatic phosphoglyceride synthesis and also a lower hepatic phosphoglyceride content. Therefore, it is suggested that this aspect of lipid metabolism be emphasized.

7625 IMMUNOCHEMICAL CHARACTERIZATION OF MITOCHONDRIA IN THE HUMAN LIVER. *(Rum.)* Benga, G. (Inst. Med. Pharm., Cluj, Rumania). *Stiinte Cercet. Biochim.* 16(3):251-260, 1973.

An immunochemical analysis was made of mitochondria isolated from human liver biopsies obtained during surgery and from rat liver. Soluble mitochondrial antigens extracted with 0.5% sodium deoxycholate were fractionated by chromatography on DEAE or TEAE cellulose and were then subjected to gel filtration through Sephadex G-150. Most of the mitochondrial protein was lipoprotein without any antigenic properties. When subjected to immunoelectrophoresis with antimitochondrial serum from rabbits, 9 precipitation lines formed, 2 in the cathode region and 7 in the anode region. Immunoelectrophoresis of mitochondrial protein obtained from a patient with persistent obstructive jaundice gave a different antigenic pattern than that obtained from normal human liver, indicating that some structural changes occur in the mitochondria in persistent jaundice. No common antigenic components were found in human and rat liver. It is concluded that reactions attributed to antimitochondrial antibodies might be crossed reactions with mitochondrial components which have no pathogenetic importance but may be useful in diagnosis.

7626 GONADOTROPIN PRODUCING HEPATOMA. *(E.)* Floyd, W. S.; Cohn, S. L. (Wayne State Univ. Sch. Med., Lathrup Village, Mich.). *Obstet. Gynecol.* 41(5):665-668, 1973.

Acute upper abdominal colicky pain radiating to the right subscapular region caused admission of a 23 yr old female at 39 weeks' gestation. Nausea and nonprojectile emesis accompanied the pain. SGOT was 36 units. On the 8th day postpartum, sudden recurrence of upper abdominal pain caused readmission. Abdominal aspiration contained blood. Laparotomy revealed both lobes of the liver were infiltrated with 1-2 cm nodules, enlarged spleen, and massive hematoma extending into the lesser sac. Continuous perfusion of 5-fluorouracil (30 mg/kg/day, i.v.) was started immediately. Liver nodule biopsy showed hepatocellular carcinoma. Irregular nests of neoplastic cells with large pale nuclei, irregular outline, prominent nucleoli, scattered mitotic figures, and focal areas of multinucleated giant cell formation were noted. Broad areas of necrosis with hemorrhage were conspicuous. The 3rd week after delivery the gonadotropin titer was greater than 7500 IU. When readmitted 6 weeks postpartum, gonadotropin levels remained at 7500-75,000 IU dilution. Methotrexate (100 mg) was started due to lack of improvement with 5-fluorouracil. No response to methotrexate was noted It was suggested that these results support the evidence of gonadotropin production in usually nonendocrine tumors.

7627 ACQUIRED DYSFIBRINOGENEMIA AND LIVER DISEASE: 30 CASES. *(Fr.)* Aiach, M.; Roge, J.; Busy, M. F.; Durand, H.; Gueroult, N.; Chanrion, C.; Leclerc, M.; Justin-Besancon, L. (Broussais Hosp., Paris, France). *Sem. Hop. Paris* 49(3):183-197, 1973.

Dysfibrinogenemia was diagnosed in 30 patients (13 men and 17 woman, aged 20-76 yr) by increased thrombin times and very low or zero optical densities in fibrinogen polymerization with reptilase. The possibility that these findings were due to low blood fibrin levels or to antithrombins V or VI was ruled out. Liver disease was diagnosed in 29 cases: alcoholic cirrhosis (18 cases), viral or probably viral hepatitis (8), Mediterranean cirrhosis (1), cirrhosis of undetermined origin (1), and adenocarcinoma superimposed on cirrhosis (1). The remaining patient had temporal arteritis (Horton's disease) with no evidence of abnormal liver function. Dysfibrinogenemia in patients with liver disease is considered acquired since the anomaly disappeared in 7 cases (in 5 of those with hepatitis and 2 of those with cirrhosis), and almost half of those with cirrhosis had no history of this anomaly. Symptoms of dysfibrinogenemia included jaundice in almost all cases, blood clotting disorders in 27 cases, and liver function disturbances in 27 cases. Although 11 of the patients had gastrointestinal, renal, nasal, and cutaneous hemorrhages, this bleeding does not appear to be caused by dysfibrinogenemia since all of these patients had other clotting disorders, particularly decreased platelet counts or major changes in the prothrombin complex. Although few biopsies and autopsies were performed, dysfibrinogenemia occurred both in individuals with very severe liver damage (subacute atrophy) and those with very minimal changes (cholestatic hepatitis). Persistence of dysfibrinogenemia was always associated with aggravation of the liver disease or failure to improve (10 patients died), while the disappearance of dysfibrinogenemia always coincided with regression of clinical and biological signs of the disease. Since these 30 cases of acquired dysfibrinogenemia were diagnosed in less than 2 yr at one hospital, it is concluded that this disorder is not as rare as was previously believed.

7628 SOME FUNCTIONAL CHANGES IN THE LIVER AND BILIARY SYSTEM IN PATIENTS WITH CHRONIC PESTICIDE POISONING. *(Rus.)* Matkovskii, S. V.; Ishchukova, M. P.; Antochanu, V. A. (no affil.). *Zdravookhr. Ross. Fed.* (1):31-34, 1973.

An investigation was made of 62 patients (48 men and 14 women, aged 20-60 yr) who had a history of occupational exposure to pesticides for 6-10 yr. Hepatitis was diagnosed in 49 of the 57 patients subjected to ^{131}I-labeled bengal rose hepatography; the remaining 8 patients had no clinical signs of hepatitis. The 49 patients with hepatitis had impaired hippuric acid synthesis, decreased serum albumin levels, and increased serum γ-, α_1-, and α_2-globulin levels. I.v. cholecystography with Bilignost demonstrated that gallbladder motility was normal in 7 and disturbed in 50 of these 62 patients; gallbladder filling did not occur in 5 cases, probably because of atony of the sphincter of Oddi. ^{131}I-labeled bengal rose hepatography, performed on 57 patients and 27 normal controls, revealed that patients with chronic pesticide poisoning of polytoxic origin had impairment of hepatic absorption and, to a lesser extent, hepatic excretion. Disturbances in gallbladder motility were found in patients with and without clinical symptoms of liver disease.

7629 SERUM ADENOSINE DEAMINASE IN LIVER DISEASE. *(Ger.)* Zipprich, B.; Nilius, R.; Otto, L.; Eismann, .; Bussen, H. J.; Peters, J. E. (1st Med. Clin., Martin Luther Univ., Halle/Saale, Germany). *Z. Gesamte Inn. Med.* 28(18):280-282, 1973.

Serum adenosine deaminase (ADA) activities were measured on 380 patients with histologically confirmed diagnoses of various hepatobiliary diseases and on 100 normal controls. These results were compared with SGOT, SGPT, and serum alkaline phosphatase activities by means of discriminant analysis. Serum ADA activities were significantly increased in acute viral hepatitis, chronic persistent hepatitis, chronic aggressive hepatitis, cirrhosis, and cholestatic liver disease but were within the normal range in patients with fatty liver, chronic reactive hepatitis, and in biliary disease with no evidence of obstruction. Serum ADA activities were normal at the onset of obstructive jaundice but, with a few exceptions, increased as the obstruction persisted. As anticipated, the greatest increase in ADA activities occurred in acute viral hepatitis. ADA was somewhat more sensitive than aminotransferase activities in diagnosing cirrhosis, was about as sensitive as SGOT and SGPT in diagnosing chronic aggressive hepatitis, and was less sensitive than aminotransferases in diagnosing chronic persistent hepatitis and cholestatic liver disease. Discriminant analysis showed that serum ADA activities were most effective in differentiating between fatty liver and chronic persistent hepatitis, between chronic aggressive hepatitis and cirrhosis, between acute viral hepatitis and obstructive jaundice (if tests on the latter group were made soon after onset of symptoms), and between acute viral hepatitis and cholestatic liver disease. In general, serum ADA activities were about as sensitive as SGPT and SGOT in diagnosing diseases which cause severe changes in the hepatic parenchyma, but ADA activities remained within normal limits when parenchymal damage was minimal.

7630 A PRELIMINARY ASSESSMENT OF THE EFFICACY OF ASANGUINEOUS-HYPOTHERMIC TOTAL BODY PERFUSION IN THE MANAGEMENT OF STAGE IV HEPATIC COMA. *(E.)* Klebanoff, G. (Wilford Hall USAF Med. Ctr., Lackland AFB, Texas). *Am. J. Gastroenterol.* 60(2):105-113, 1973.

Hepatic coma was treated by asanguine, hypothermic total body perfusion in 12 patients (8 males and 4 females, aged 16-47 yr). Diagnoses included Laennec's cirrhosis (1), Reyes syndrome (2), hepatitis (6), Wilson's disease (1), and chronic and acute hepatitis (2). All were in Stage IV hepatic coma. Irreversible shock caused 1 death in the operating room. No neurologic or psychiatric function impairment could be attributed to total body perfusion. No deleterious effects were observed on other normal organs in the body undergoing perfusion. The results suggest the following trends. On patients in Stage IV coma secondary to Reyes syndrome, or viral hepatitis, who are not brain dead, total body perfusion will bring about a definite improvement in the level of consciousness, a great reduction in biochemical abnormalities identifiable by serology, and a greatly improved renal function. If a patient, after rising to Stage II coma, has no sustained improvement of level of consciousness or liver function, the likelihood of total hepatic necrosis is strong. Although the prognosis is poor, it is suggested that, in such cases, a second total body perfusion be performed for the purpose of preparing the patient for an auxiliary hepatic allograft. The unadjusted survival rate for this small group was 4 of 12 patients, or

33 1/3%. However, considering that 3 patients were already brain dead, 1 had irreversible shock, and 1 was mistakenly given noncolloid perfusate, the corrected survival rate was 4 of 7 patients, or 56%, and all deaths were associated with total hepatic necrosis.

7631 BENIGN LIVER CELL TUMORS. CLASSIFICATION AND ULTRASTRUCTURAL PATHOLOGY. *(E.)*

Phillips, M. J.; Langer, B.; Stone, R.; Fisher, M. M.; Ritchie, S. (Toronto Gen. Hosp., Canada). *Cancer* 32(2):463-470, 1973.

The pathologic features of 15 benign liver cell tumors from 10 patients have been studied. Distinctive gross, microscopic, and ultrastructural features serve to distinguish 2 pathologic entities: liver cell adenoma (4) and hepatic hamartoma (11). Both conditions are benign tumors and must be differentiated from primary liver cell carcinoma. Hepatic hematoma differs from liver cell adenoma in that the later has cytologic evidence of malignancy and it differs from cirrhosis which is a diffuse hepatic lesion. To differentiate liver cell adenoma from liver cell carcinoma is more difficult. If a liver cell tumor is encapsulated and entirely composed of highly differentiated histologically normal hepatocytes, and if mitosis and evidence of capsular or blood vessel invasion are absent, the lesion is clinically benign and identified as liver cell adenoma. It is proposed that the term hepatic hamartoma be used for that common focal nodular malformation of the liver that is composed of hepatocytes and biliary epithelial cells, and that the term liver cell adenoma be reserved for those benign neoplasms composed solely of well-differentiated hepatocytes.

7632 DEMONSTRATION OF PORPHYRINS IN CEREBROSPINAL FLUID IN CHRONIC HEPATIC PORPHYRIA.

(E.) Filippini, L.; Simmler, F. (Med. Clin., Cantonal Hosp., Lucerne, Switzerland). *Germ. Med.* 3(1):13-14, 1973.

Liver biopsy was performed on a 49-year-old male cerebrovascular accident patient who exhibited hepatomegaly and a mild increase in transaminase activity. A diagnosis of porphyria cutanea tarda, now dermatologically inactive, was made. Thin-layer chromotography and spectral photometry of porphyrins in urine and cerebrospinal fluid were undertaken. Uro- and hepatacarboxy-porphyrin were demonstrated in the cerebrospinal fluid. Compared with the urinary findings, however, there were no hexacarboxy-, pentacarboxy-, and copro-porphyrins in cerebrospinal fluid. These results demonstrate that uro- and heptacarboxy-porphyrin apparently can pass the blood-brain area. A direct relationship between the cerebrovascular accident and the porphyrin content in cerebrospinal fluid appears unlikely. The demonstration of porphyrins in CSF could be of practical importance if further studies demonstrate that in cases of porphyria without porphyrinuria diagnostically adequate amounts of porphyrin are found in CSF.

7633 WILSON'S DISEASE: IDENTIFICATION OF AN ABNORMAL COOPER-BINDING PROTEIN. *(E.)*

Evans, G. W.; Dubois, R. S.; Hambidge, K. M. (Human Nutr. Lab., Agricult. Res. Serv., U.S. Dept. Agricult., Grand Forks, N.D.). *Science* 181(4105):1175-1176, 1973.

Liver samples were taken from 2 teenage symptomatic Wilson's disease patients and 2 teenage controls with elevated hepatic copper due to biliary cirrhosis. After purification and isolation of ^{64}Cu-labeled metallothionein, the apoprotein, thionein, was prepared from which copper-thionein was in turn prepared by equilibrium dialysis. Even though thionein from both groups contained the same number of copper-binding sites, the copper-binding constant for the protein from Wilson's disease patients was 4 times that from controls. It is noted that an abnormal protein with increased affinity for copper would explain many of the defects in copper hemeostasis in hepatolenticular degeneration, especially in asymptomatic patients. It is suggested that increased binding affinity of th temporary storage protein in the hepatocyte of Wilson' disease patients probably shifts the normal equilibrium of the hepatic copper pool, causing depressed biliary copper excretion and decreased incorporation of copper into ceruloplasmin. As the disease advances, the binding sites on the storage protein become saturated, and excess metal is ingested by hepatic lysosomes. Saturation of the hepatic copper-binding sites causes decreased uptake of metal with concomitant elevation in plasma copper not bound to ceruloplasmin. It is not known if the increased deposition of copper in extrahepatic tissues results from elevated non-ceruloplasmin copper or from presence of the abnormal protein in these organs.

7634 TRANSJUGULAR APPROACH TO LIVER BIOPSY AND TRANSHEPATIC CHOLANGIOGRAPHY. *(E.)*

Rosch, J.; Lakin, P. C.; Antonovic, R.; Dotter, C. T. (Univ. Oregon Med. Sch., Portland). *N. Engl. J. Med.* 289(5):227-231, 1973.

The percutaneous transjugular approach to liver biops and cholangiography was used in 61 patients (33 males and 28 females, average age 58 yr). Biopsy and cholangiography were each performed in 36 patients, liver biopsy alone in 8, and cholangiography alone in 17. In 39 patients (89%) diagnostic biopsy specimens were obtained. Cholangiography succeeded in 29 of 31 patients (93%) with enlarged intrahepatic ducts. The transjugular approach can not be used when occlusions of the internal jugular veins and anomalies or obstructions of superior or inferior vena cava exist. Difficulties also occurred in cases where hepatic veins entered the inferior vena cave at a sharp angle The stiff needle could not make the curve and enter the liver. The safety of this approach is stressed and it is recommended as complementary to the standard transperitoneal route in liver biopsy, particularly in the presence of coagulopathy, high-grade obstructive jaundice, or major ascites. For cholangiography, the transjugular route is preferable to the standard transperitoneal technique.

7635 ISOENZYMES OF SERUM ALKALINE PHOSPHATASE IN RATS DURING EXPERIMENTAL HEPATOBILIARY DAMAGE AND RICKETS. *(Ukr.)* Hromashevs'ka, L. L.; Iavors'kyi, I. H. (Kiev Sci. Res. Inst. Infectious Dis., USSR). *Ukr. Biokhim. Zh.* 45(1):65-69, 1973.

Isoenzymes of alkaline phosphatase were investigated in serum and in homogenates from the liver, small intestine, and bone of normal rats and of rats with toxic hepatitis (induced by 0.5 ml/100 g of carbon tetrachloride, s.c.), obstructive jaundice (induced by ligation of the common bile duct), and rickets (induced by feeding a calcium-deficient diet for 1.5 months). Total alkaline phosphatase activity and the activities of its isoenzymes were measured on native serum and on serum inactivated by heating to 56 C for 15 min. Isoenzymes were separated by vertical electrophoresis in 0.005 M tris-glycerine buffer at pH 8.3 on 7% polyacrylamide gel at 4-6 C for 4 hr with a current of 2 milliamps. Enzyme fractions on the gel were developed with a lead reaction using sodium β-glycerophosphate as the substrate. By means of heat inactivation experiments it was demonstrated that alkaline phosphatase activity present in serum of normal rats originated in the small intestine, bone, and liver. Total alkaline phosphatase activity in native serum averaged 14.9 ± 1.3 Bodansky U, while that in inactivated serum averaged 6.1 ± 0.9 Bodansky U. It has been previously demonstrated that isoenzymes from the bone and liver are heat-liable, while those from the small intestine are heat-stable. In rats with toxic hepatitis the mean activity of total serum alkaline phosphatase increased to 31.3 ± 0.7 Bodansky U; this increase was primarily due to increases in alkaline phosphatase from the liver and intestine. Total alkaline phosphatase activity in the serum of rats with obstructive jaundice increased to a mean of 25.3 ± 1.2 Bodansky U and consisted primarily of an increase in the rapidly migrating anode fraction.

7636 CORTICOSTEROID-INDUCED CHANGES IN UREA METABOLISM IN PATIENTS WITH HEPATOCELLULAR DISEASE. *(E.)* Jones, E. A.; Cain, G. D.; Dickinson, G. (Roy. Free Hosp., London, England). *Gastroenterology* 62(4):612-617, 1972.

Quantitative studies of urea metabolism were made by a kinetic technique using ^{13}C urea in 8 patients with hepatocellular disease before and after a 13-day course of prednisolone (0.75 to 1 mg/kg/day, with maintenance dose at less than 15 mg/day). Diagnoses in the 8 patients (3 males and 5 females, aged 27-71 yr) included alcoholic cirrhosis (1), cryptogenic cirrhosis (4), chronic aggressive hepatitis (1), chronic persistent hepatitis (1), and cholestatic hepatitis (1). The duration of the illness ranged from 0.3-15 yr. Total bilirubin ranged from less than 0.5 to 26.0 mg/100 ml; alkaline phosphatase ranged from 16-57 King-Armstrong U. After treatment the mean plasma urea concentration was higher in every case, the increases varying between 4-22 mg/100 ml. The initial mean absolute synthetic rate of urea (228 mg/kg/day) was 45% lower than that in 2 control subjects. Treatment with prednisolone caused a 109% increase in the mean absolute synthetic rate of urea (to 476 mg/kg/day). This therapy was associated with an episode of hepatic coma in 1 patient and with clinical signs of hepatic precoma in 3 others. It is inferred that the liver in patients with hepatocellular disease usually has the capacity to increase the synthetic rate of urea appreciably in response to an appropriate stimulus. The data can be adequately explained in terms of the known effects of corticosteroids on nitrogen metabolism including the catabolic effect of these drugs on protein metabolism in peripheral tissues. The results imply that corticosteroids increase the turnover of nonprotein nitrogenous compounds of small molecular weight, including ammonia, in patients with liver disease.

7637 LOCALIZATION OF RAT LIVER α-FOETOPROTEIN BY CELL AFFINITY LABELLING WITH TRITIATED OESTROGENS. *(E.)* Uriel, J.; Aussel, C.; Bouillon, D.; de Nechaud, B.; Loisillier, F. (Inst. Sci. Res. Cancer, Villejuif, France). *Nature [New Biol.]* 244(136):190-192, 1973.

By means of cell affinity labeling with tritiated estrogens, observations were made on the localization of rat liver α-fetoprotein in fetuses, neonates, and adult animals bearing primary hepatomas induced by chemical carcinogens. Wistar rat fetuses and neonates were killed by decapitation and adult animals by exsanguination under ether anesthesia. The livers were promptly removed and processed. The intracellular pattern of labeling with estrogens was the same in fetal and neonatal livers as in hepatocellular carcinomas. Tumor nodules from 5 induced hepatocellular carcinomas were examined. After incubation in tritiated estrogens, radiolabeled cells were found in 4 tumors from animals with detectable levels of serum α-fetoprotein. The cell type producing α-fetoprotein is most probably a transitional liver cell distinct from either normal or neoplastic hepatocytes and present in hepatocellular carcinomas as well as in fetal and neonatal liver. Whether this cell persists in normal adult liver in a resting state and becomes an α-fetoprotein producer under certain stimuli or represents a transitory stage of differentiation of a given precursor cannot be elucidated from present data.

7638 LIVER CELL DYSPLASIA: A PREMALIGNANT CONDITION. *(E.)* Anthony, P. P.; Vogel, C. L.; Barker, L. F. (Middlesex Hosp. Med. Sch., London, England). *J. Clin. Pathol.* 26:217-223, 1973.

Liver cell dysplasia is defined as cellular enlargement, nuclear pleomorphism, and multinucleation of liver cells occurring in groups or occupying whole cirrhotic nodules. The prevalence, natural history, and relation to the Australia or hepatitis-associated antigen (HAA) have been studied in 552 Ugandan African patients with normal, cirrhotic, and cancerous livers. Liver cell dysplasia was found in only 2 of 200 (1%) patients with normal livers, in 3 of 43 (6.9%) of patients with normal livers bearing primary liver cell carcinoma, 35 of 175 (20.3%) patients with cirrhosis, and 80 of 124 (64.5%) of patients with cirrhosis and primary liver cell carcinoma. In 32 (71.1%) of 45 cirrhotics with liver cell carcinoma, tests for alpha fetoprotein were positive. Cirrhotic patients without dysplasia were, on average, 10 yr younger than those with dysplasia and the latter were on average 6 yr younger than those with cirrhosis and carcinoma. Liver cell dysplasia occurred more frequently in males than in females. It was found in all but one instance in macronodular or mixed forms of cirrhosis only. There was a strong relation between dysplasia and the presence of HAA in 104 patients that suggests a possible carcinogenic mechanism for the long-incubation (serum or B) hepatitis virus in liver cell carcinoma. It is concluded that the presence of liver cell dysplasia identifies a group of patients with a high risk of liver cell carcinoma and that they should be followed up by serial alpha fetoprotein estimations.

7639 HEPATIC ALTERATIONS IN HODGKIN'S DISEASE.

(E.) Davey, F. R.: Doyle, W. F. (Letterman Gen. Hosp., San Francisco, Calif.). *N.Y. State J. Med.* 74(15):1981-1986, 1973.

A clinicopathologic analysis of livers in 78 patients with Hodgkin's disease revealed intrahepatic Hodgkin's disease in 41 (70%) of the 59 studied at autopsy and in 4 (12%) liver biopsies. Statistically, Hodgkin's disease infiltrates were found in the spleen, periaortic lymph nodes, porta hepatic and other retroperitoneal lymph nodes, and in bone marrow more frequently in Hodgkin's disease-involved livers than in uninvolved livers. Massive hepatic Hodgkin's disease infiltrates were often associated with abnormal liver function tests, jaundice, and hepatomegaly. Hodgkin's disease was mainly located in portal areas, especially when the lesion was microscopic. Terminally, the infiltrates were associated with marked portal fibrosis and focal hepatonecrosis. In 9 autopsied cases (23%), invasion of intrahepatic portal veins was noted. In 5 (15%) of biopsied cases, tissue sections showed sarcoid-like granulomas and in 8 (24%) nonspecific portal inflammation was noted. Microscopic examination of the liver is the best way to identify intrahepatic Hodgkin's disease. The differential diagnosis of liver dysfunction in Hodgkin's disease patients may only be possible by liver biopsy.

7640 ABO BLOOD GROUPS IN PRIMARY CARCINOMA OF THE LIVER.

(E.) Chew, B. K.; Seah, C. S.; Ong, Y. W.; Tan, L. (Dept. Med., Univ. Singapore). *Aust. N.Z. J. Med.* 3(2):129-130, 1973.

The distribution of ABO blood groups among 214 Chinese patients with primary carcinoma of the liver was compared with the distribution among a control series of Chinese blood donors (15,279) in Singapore. No relationship was revealed between ABO blood groups and primary carcinoma of the liver. The proportion of group A subjects was higher among the liver cancer patients (31.3%) than among the controls (26%), but the difference was not statistically significant.

7641 ELECTROPHORETIC VARIANTS OF ALANINE AMINOPEPTIDASE IN SERUM IN HEPATOBILIARY DISEASES.

(Ger.) Peters, J. E.; Nilius, R.; Otto, L. (Inst. Clin. Biochem., Martin Luther Univ., Halle/Saale, Germany). *Clin. Chim. Acta* 45(2):177-187, 1973.

Electrophoretic patterns of alanine aminopeptidase (AAP) were investigated in serum from 696 patients with hepatobiliary diseases and in 396 controls with other diseases but not evidence of hepatobiliary disease. While normal subjects have only one AAP fraction in the α_1-globulin region, about 35% of the patients with hepatobiliary disease, but only 3% of the controls had additional AAP fractions. Follow-up examinations of the 10 controls with abnormal AAP patterns showed that most had undiagnosed biliary disease. Additional anode fractions were the most common variants of electrophoretic AAP patterns. In addition to increased activities, all AAP variants from patients with hepatobiliary disease had a lower mobility than the normal serum enzyme. These changes in AAP patterns were typical but not specific for the diseases and disease groups studied. Abnormal AAP patterns occurred in about 81% of the patients with biliary diseases (obstructive jaundice, cholestatic liver disease, secondary biliary cirrhosis, hepatic metastases, tumor infiltration, anicteric biliary disease). This suggests that biochemical changes produced by or associated with cholestasis can cause changes in the electrophoretic mobility of AAP by producing changes in the enzyme molecule. Normal AAP patterns were found in extrahepatic obstructive jaundice and biliary cirrhosis. Although abnormal patterns occurred in patients with moderately and slightly elevated AAP activities, the electrophoretic pattern of AAP was not consistently abnormal in patients with high AAP activities; normal patterns were often found in diseases involving the hepatic parenchyma (hepatitis, cirrhosis, fatty liver). If abnormal AAP patterns did occur in hepatitis, they were not present at the onset but appeared during the 3rd week or later. Of the patients with biliary disease, 32 also had pancreatitis or pancreatic malignancies; none had an AAP pattern specific for pancreatic disease.

7642 LIVER DISEASE IN MULTIPLE MYELOMA. *(E.)*

Thomas, F. B.; Clausen, K. P.; Greenberger, N. J. (Ohio State Univ. Coll. Med., Columbus). *Arch. Intern. Med.* 132(2):195-202, 1973.

Necropsies of 64 patients (40 males and 24 females; mean age at diagnoses, 56.1 and 60.8 yr, resp.) with multiple myeloma were reviewed. Hepatomegaly was present in 58% of cases and splenomegaly in 25%.

Jaundice occurred in 9 patients with bilirubin values ranging between 3.2-17.3 mg/100 ml. Exudative ascites was present in 9 patients, including 6 without associated peritoneal disease. Increased BSP retention, hypoalbuminemia, and hypoprothrombinemia were frequently present. On final admission SGPT ranged from 100-400 U/100 ml; SGOT, from 20-900 U/100 ml; serum alkaline phosphatase, 3.8-37 U, and serum bilirubin levels, 0.3-11.3 mg/100 ml. Plasma cell infiltration of the liver occurred in 40% of cases, usually as either tumor-forming nodules or diffuse sinusoidal infiltration. The data obtained indicate that abnormalities in tests of liver function and extensive plasma cell infiltration of the liver are common findings in multiple myeloma, and that jaundice and exudative ascites occur with surprising frequency in this disorder.

7643 CARCINOMA OF THE HEPATIC DUCTS: REVIEW OF 11 CASES. *(E.)* White, T. T. (Univ. Hosp., Seattle, Wash.). *Am. Surg.* 39(8):445-447, 1973.

A study was made of 11 patients having carcinomas of the extrahepatic bile ducts in whom the carcinomas were located in the upper hepatic ducts and their bifurcation. All appeared to have obstructive jaundice. At the initial operation the cause of jaundice was diagnosed as sclerosing cholangitis (7 cases), retroperitoneal fibrosis (1), and carcinoma of the upper bile ducts (3). Carcinoma was diagnosed at the second operation in 8 patients, at the third in 2, and at autopsy in 1. Treatment included resection of the tumor with anastomosis of the residual ducts to the intestine (1, still alive 23 months after operation); drainage by T-tube alone (7, average survival time 7.4 months), or by hepaticojejunostomy (3, average survival time 16 months). In all tumors cholangitis was the principal complication. It is suggested that curettage of the inside of the bile duct with a scoop may be an effective approach to accurate diagnosis of the carcinoma. Percutaneous transhepatic cholangiography is the most effective routine method of making this diagnosis in the deeply jaundiced patient. Radical excision, if at all possible, should be performed with anastomosis of the hepatic ducts to the jejunum. When prolonged T-tube drainage is necessary, silastic tubes may be more appropriate than rubber tubes. In cases where it is impossible to thread tubes from below up into the liver, intrahepatic hepaticojejunostomy is suggested. Earlier diagnosis will permit more radical procedures.

7644 VALUE OF DETERMINING SERUM LEUCINE ARYL AMIDASE ACTIVITY IN GASTROINTESTINAL DISEASE. *(Fr.)* Tamarelle, C.; Quinton, A.; Bancons, J.; Cuzon, J.; Dubarry, J. J. (St. Andre Hosp., Bordeaux, France). *Arch. Fr. Mal. App. Dig.* 62(3):225-233, 1973.

The leucine arylamidase (LAA) activity of leucine aminopeptidase was determined on serum from 64 controls with normal liver function by using leucyl p-nitroanilide as a substrate. Determinations were made by incubating 0.2 ml serum with 2.5 μM of leucine p-nitroaniline in 2.2 ml of 0.05 M phosphate buffer at pH 7.2 and 37C. The reaction was stopped by adding 0.5 ml of 30% acetic acid, and the optical density was read at 410 nm against a blank containing no substrate. Since p-nitroaniline does not follow Beer-Lambert's law, a kinetic method was used. The mean activity of LAA in these controls was 28.9 ± 9.8 International milliunits/liter. The mean value for males was higher than that for females, but the difference was not significant. Serum LAA activities were also determined on 242 sera from 206 patients with gastrointestinal diseases. LAA activities increased slightly in cirrhosis, increased progressively in protracted hepatitis, and increased significantly in fatty liver and cholestasis of extrahepatic origin. While normal values were obtained in nonhepatic cancer, LAA was consistently increased in liver cancer. No increases occurred in LAA values in acute and chronic pancreatitis or in bone diseases in which alkaline phosphatase was increased (Paget's disease, secondary bone cancer). It is concluded that LAA activities give more specific information about cholestasis than alkaline phosphatase values.

7645 CYSTATHIONINE EXCESS IN CHILDREN WITH HEPATIC CANCER. *(E.)* Helson, L.; Peterson, R. H. F.; Schwartz, M. K. (Mem. Hosp. Cancer Allied Dis., New York, N.Y.). *Cancer Res.* 33(7):1570-1573, 1973.

Previous observation of cystathioninuria in 7 male children with hepatoblastoma are extended to an examination of 5 additional children (3 female and 2 male, aged 4 1/2 mo to 15 yr), 3 having hepatoplastoma, 2 having hepatocellular carcinoma. Automated chromatography was used to measure the 24-hr urinary excretion of cystathionine in all subjects, and thin-layer chromatography to detect the compound in metastatic tumor tissue of 2 subjects. Increased cystathioninuria was present in 3 patients at the time of diagnosis and 2 developed it during the course of their disease. Urinary excretion levels decreased following effective therapy and increased with recurrence of tumor in 1 patient. The lack of correlation between elevated urinary cystathionine excretion and tumor volume and the presence of elevated urinary cystathionine levels in neuroblastoma limit its potential as a screening method.

7646 DEVELOPMENT OF CHRONIC CHOLANGITIS AND PANCREATITIS IN PATIENTS WITH CONGENITAL ANOMALIES OF THE LIVER AND PANCREAS. *(Ger.)* Wanger, F.; Amgwerd, R. (Cantonal Hosp., St. Gallen, Switzerland). *Z. Gastroenterol.* 10(5):339-348, 1972.

7647 α_1-ANTITRYPSIN DEFICIENCY WITH LIVER DISEASE AND IRON OVERLOAD. *(Ger.)* Kroner, T. (Canton Hosp., Winterthur, Switzerland). *Schweiz. Med. Wochenschr.* 103(34):1192-1195, 1973.

7648 LARGE CAVERNOUS ANGIOMA OF THE RIGHT LOBE OF THE LIVER. *(Fr.)* Paris, J.; Ribet, M.; Paris, J. C.; L'Hermine, C.; Houcke, M. (Univ. Hosp. Ctr., Lille, France). *Sem. Hop. Paris* 49(18):1309-1310, 1973.

7649 CHANGES IN THE LIVER AFTER INTRAPERITONEAL RADIOGOLD THERAPY. *(Ger.)* Morgenroth, K.; Verhagen, A.; Simons, F. K. (Radiol. Clin., Univ. Bonn, Germany). *Strahlentherapie* 145(3):282-288, 1973.

7650 ATTEMPT TO EVALUATE THE FUNCTIONAL STATUS OF THE LIVER IN NEWBORNS. *(Ger.)* Karakaschoff, A. W.; Kisselkova, V.; Stomonjakova, S.; Uzunova, T. (Pediatric Res. Inst., Sofia, Bulgaria). *Wissensch. Z. Friedrich Schiller Univ.* 24(4):717-721, 1972.

7651 ADVANCES IN THE FIELD OF LIVER DISEASE. *(Ger.)* Strohmeyer, G. (Med. Clin., Univ. Marburg/Lahn, Germany). *Z. Gastroenterol.* 10(1):2-16, 1972.

7652 LIVER CELL MORPHOLOGY IN PHASE CONTRAST ILLUMINATION. *(Rus.)* Livshits, E. A. (Rep. Oncol. Dispensary, Karelian ASSR, USSR). *Lab. Delo* (2):98-100, 1973.

7653 BIOCHEMICAL CHANGES OF THE LIPID IN BIOPSIED LIVERS OF PATIENTS WITH MALIGNANT NEOPLASTIC DISEASES. *(E.)* Nakazawa, I.; Yamagata, S. (Tohoku Univ. Sch. Med., Sendai, Japan). *Med. Chir. Dig.* 2(1):19-23, 1973.

7654 DISTURBANCES OF FIBRIN CLOTTING IN CHRONIC LIVER DISEASES AND DYSPROTEINEMIAS. *(Ger.)* Braun, K.; Wenzel, E.; Breddin, K. (Med. Clin., Rhine-Westphalian Technical Coll., Aachen, Germany). *Med. Welt* 23(40):1390-1392, 1972.

7655 HAMARTOMAS OF THE LIVER. *(Fr.)* Leger, L.; Cachin, M.; Chapuis, Y.; Delaitre, B.; Launois, P.; de Saint-Maur, P. P.; Bonnin, A. (Cochin Hosp., Paris, France). *Nouv. Presse Med.* 2(6):353-358, 1973.

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7715 PRIMARY CANCER OF THE LIVER IN ADULTS: SURGICAL TREATMENT BY PARTIAL HEPATECTOMY. *(Fr.)* Moreaux, J.; Veyrieres, M.; Hepp, J. (no affil.). *Arch. Fr. Mal. App. Dig.* 61(12):801-802, 1973.

7716 MORPHOLOGICAL CHANGES IN THE LIVER IN PERIARTERITIS NODOSA. *(Rus.)* Skorodumova, N. P. (Donetsk Med. Inst., USSR). *Vrach. Delo* (7): 59-61, 1973.

See also, 6705, 6707, 6711, 6716, 6720, 6722, 6725, 6726, 6731, 6732, 6736, 6740, 6743, 6745, 6746, 6749, 6751, 6756, 6758, 6759, 6766, 6767, 6773, 6782, 6783, 6784, 6786, 6788, 6803, 6805, 6808, 6815, 6817, 6822, 6831, 6832, 6841, 6845, 6846, 6848, 6851, 6855, 6856, 6857, 6863, 6871, 6876, 6882, 6885, 6886, 6891, 6892, 7059, 7060, 7085, 7188, 7226, 7277, 7406, 7422, 7431, 7499, 7502, 7551, 7936, 7928, 7948, 7949, 7983, 8033, 8034, 8057, 8111, 8138, 8157, 8159, 8164, 8188, 8195, 8200, 8202.

LIVER AND BILIARY TRACT

Hyperbilirubinemic States

7717 PHENOBARBITAL EFFECT ON SERUM BILIRUBIN LEVELS IN UNDERWEIGHT INFANTS. *(E.)* Cao, A.; Falorni, A.; Francassini, F.; Lungarotti, M. S. (Clin. Pediatr., Univ. Perugia, Italy). *Helv. Paediatr. Acta* 28(3):231-238, 1973.

The effect of phenobarbital (3 mg/kg, p.o. or i.m., twice a day) on serum bilirubin levels was evaluated in 179 infants with a birth weight of 2.5 kg or less and/or a gestational age of less than 38 weeks.
Of these infants, 120 had an appropriate birth weight for their gestational age and 59 were small for their gestational age. Controls consisted of 184 untreated infants (120 with appropriate birth weights and 64 with low birth weights). Ten pairs of monozygotic twins were included. In the entire group of treated

patients, phenobarbital decreased bilirubin levels significantly on the 4th day and reduced the incidence of bilirubin levels higher than 12 mg/100 ml. Bilirubin levels decreased significantly on the 4th day in infants with appropriate birth weights and on the 6th day in those with low birth weights. No correlation was found between the effect of phenobarbital and gestational age in infants with a gestational age of 32 weeks or less. In infants with a gestational age of more than 32 weeks a clear correlation was found: the more advanced the gestational age, the more prompt the effect of phenobarbital. These findings suggest that phenobarbital induction of bilirubin glucuronyl transferase and/or anion binding protein is correlated with the maturity of the fetal liver at birth. Side effects of phenobarbital on general behavior, motor activity, feeding, respiration, and reflexes were not observed.

7718 DOES DRUG THERAPY INCREASE THE RISK OF KERNICTERUS IN NEWBORNS? *(Ger.)* Windorfer, Jr., A.; Mihailova, K.; Pringsheim, W. (Pediatric Clin., Univ. Freiburg/Breisgau, Germany). *Dtsch. Med. Wochenschr.* 98(25):1260-1267, 1973.

Free bilirubin was measured in solutions of human albumin and sera from 10 newborns which had been incubated at pH 7.4, 7.1, and 6.9 with 100 µg/ml of ampicillin, carbenicillin, colistin, cephalothin, erythromycin, gentamycin, oxacillin, diazepam, phenobarbital, or promoter for diazepam solution. The ratio of albumin:bilirubin was adjusted to 1:2. In all cases more free bilirubin was found in solutions of human albumin than in newborn sera. Free bilirubin levels were higher in alkaline than in acid media with both albumin solutions and newborn sera. This is attributed to the decreased solubility of bilirubin in acid media. After incubation with 100 µg/ml of diazepam at pH 7.4, 7.1, and 6.9, free bilirubin levels were also determined in sera from (1) premature infants weighing less than 2500 g, (2) newborns weighing 2500 g or more, (3) infants aged 2-11 months, and (4) children aged 1-5 yr. There was a significant difference between free bilirubin levels in premature and new born infants at pH 7.4 and 7.1. Free bilirubin levels were significantly higher in sera from premature infants, particularly those weighing less than 2000 g. It is recommended that diazepam and oxacillin not be used in the treatment of premature infants.
To prevent the development of kernicterus, human albumin should be administered along with the drug to form conjugates with any free bilirubin produced by diazepam or oxacillin if no other drugs can be substituted.

7719 OPTIMAL OROTIC ACID DOSE FOR PREVENTION OF TOXIC HYPERBILIRUBINEMIA IN PREMATURE INFANTS. *(Ger.)* Hinkel, G. K.; Kintzel, H. W. (Carl Gustav Carus Med. Acad., Dresden, Germany). *Acta Paediatr. Acad. Sci. Hung.* 13(4): 367-375, 1972.

Orotic acid (100-500 mg/day p.o. in 2-3 doses) was administered for the first 6 days after birth to 316 premature neonates weighing 1000 to 2500 g at birth; 52 untreated premature neonates served as controls. Since a previous study showed that orotic acid did not reduce serum bilirubin concentrations in mature neonates, infants with birth weights of less than 2500 g and a minimum gestation age of 37 weeks were excluded. Direct and indirect serum bilirubin values were measured on days 3-6, and exchange transfusions were performed if the unconjugated bilirubin exceeded 18 mg/100 ml. While 100 mg/day of orotic acid had little effect on serum bilirubin concentrations, 200-500 mg/day caused significant decreases and reduced the necessity for performing exchange transfusions. The optimum dose was 200 mg/kg/day. Unconjugated bilirubin values of more than 18 mg/100 ml occurred in 28.8% of the untreated controls, but in only 5.6% of the neonates treated with orotic acid. In contrast to phenobarbital, the use of orotic acid in these doses caused no side effects. Mortality was the same in infants treated with orotic acid and in untreated controls. The action of orotic acid on serum bilirubin concentrations in premature neonates is attributed to an increase in the synthesis of coenzyme or nucleic acids.

7720 RELATIVE ROLES OF PHOTOTHERAPY AND PHENOBARBITONE IN TREATMENT OF NONHAEMOLYTIC NEONATAL JAUNDICE. *(E.)* Wong, Y. K.; Wood, B. S. B. (Queen Elizabeth Med. Ctr., Birmingham, England). *Arch. Dis. Child.* 48(9):704-708, 1973.

A comparison was made of the effectiveness of phenobarbital (8 mg/kg/day, i.m., of phenobarbital sodium with propylene glycol as a vehicle in 3 divided doses/day for a total of 10 doses) and phototherapy for 60 hr in the treatment of 61 infants with plasma bilirubin levels over 15 mg/100 ml. Since the known mechanisms for alleviation of jaundice by phenobarbital and phototherapy are unrelated, the effect of combined therapy was also investigated. Infants were excluded if they had rhesus hemolytic disease, any evidence of infection, diabetic mothers, A or B blood groups and group O mothers, or were being breast fed. Within 24 hr after institution of therapy, the group receiving phototherapy alone or phototherapy plus phenobarbital had significantly lower bilirubin levels than either the controls or the phenobarbital group; this lower level was maintained at 60 hr. In infants with birth weights over 2.5 kg bilirubin levels fell no faster than in controls up to 60 hr, but at 84 hr bilirubin values were about the same as in other treated groups. In infants weighing 2.5 kg and under this decrease did not occur, even at 84 hr, indicating that the effect of phenobarbital is too slow to control a rising bilirubin level once it has reached 15 mg/100 ml or more. Deaths occurred in 2 infants treated with a combination of phototherapy and phenobarbital: one resulted from septicemia and the other from meningitis. Phenobarbital may have masked symptoms in the latter case. It is suggested that contradictory results in the literature may be due to variable absorption or vomiting of phenobarbital administered p.o. Because phenobarbital is virtually insoluble in water, most preparations contain ethanol which also acts as an enzyme inducer; propylene glycol, the vehicle used in these studies, has no such action.

7721 NEONATAL JAUNDICE AND MATERIAL OXYTOCIN INFUSION. *(E.)* Davies, D. P.; Gomersall, R.; Robertson, R.; Gray, O. P.; Turnbull, A. C. (Welsh Natl. Sch. Med., Cardiff, Wales). *Br. Med. J.* 3(5878):476-477, 1973.

A prospective study of 78 neonates suggests an association between maternal oxytocin infusion and neonatal jaundice. On the 2nd and 5th days 36 infants of mothers whose labor had been induced by amniotomy followed immediately by oxytocin (average infusion rate 16.8 mU/min, i.v., for 7 hr 20 min) had mean total bilirubin levels significantly higher than did 28 infants whose mothers had had a spontaneous onset of labor and did not require oxytocin. Bilirubin levels in 14 infants of mothers whose onset of labor was spontaneous but required oxytocin (average infusion 12.0 mU/min for 5 hr 15 min) to accelerate progress did not differ significantly from those who had not received oxytocin. These findings suggest a dose-dependent effect of oxytocin, however, those mothers whose labor was artificially induced had more frequently been given nitrazepam and bupivacaine than had mothers in other groups. It is also suggested that the corticosteroid status of the infant may be the important link in this study, in that a level of relative enzyme immaturity in the offspring of women who do not enter parturition spontaneously would affect the adrenocorticosteroids and in turn the ability of the neonate liver to manage the early postnatal bilirubin load.

7722 PHENOBARBITAL IN NEONATAL JAUNDICE. *(Cz.)* Hoskova, A.; Hlavon, J.; Palenikova, K.; Patkova, A. (Med. Fac., J. E. Purkinje Univ., Brno, Czechoslovakia). *Cesk. Pediatr.* 28(1):41-43, 1973.

Of 92 healthy full-term newborns with no signs of blood-group incompatibility, 31 received no medication, 30 were given 1/2 of a Hysteps tablet 3 times a day (2.5 mg/day phenobarbital p.o.), and 31 received 8 mg phenobarbital 3 times a day (24 mg/day phenobarbital) i.m. Phenobarbital treatment was continued for 10 days. Serum bilirubin concentrations in newborns given phenobarbital i.m. for 4 days were significantly lower than in controls. At the dose used in this study, Hysteps had no effect on serum bilirubin concentrations. After 4 days, serum bilirubin concentrations were significantly lower than those found in cord blood in 10 of the 31 newborns given phenobarbital i.m.; this was true in only 1 of the other 61 newborns. The failure of phenobarbital administered p.o. to lower serum bilirubin concentrations is attributed to the low solubility of phenobarbital in aqueous media and the slow absorption of suspended tables in the gastrointestinal tract of newborns.

7723 THE ADDITIVE ACTION OF A COMBINATION OF ENZYME INDUCERS (PHENOBARBITAL/NIKETHAMIDE) ON THE SERUM BILIRUBIN LEVEL IN NEWBORNS. *(Ger.)* Kintzel, H. W.; Schwarze, R.; Hinkel, G. K. (Carl Gustave Carus Med. Acad., Dresden, Germany). *Wissensch. Z. Friedrich Schiller Univ.* 21(4):739-742, 1972.

Since phenobarbital depresses the respiratory center when administered in doses large enough to prevent hyperbilirubinemia (100 mg/kg/day), phenobarbital was combined with nikethamide, a respiratory stimulant and microsomal enzyme inducer, to prevent hyperbilirubinemia in 280 clinically normal, full-term newborns. Phenobarbital (100 mg/kg/day divided into 2 doses/day for 5 days) was administered p.o. to 62 newborns; 59 newborns received the same dose of phenobarbital + nikethamide (60 mg/kg/day) divided into 6 doses for 5 days); 53 received the same dose of phenobarbital + a larger dose of nikethamide (100 mg/kg/day for 5 days); and 106 newborns received no medication. Serum total and indirect bilirubin concentrations were measured on all newborns on days 3-5. Phenobarbital alone decreased serum bilirubin concentrations, particularly on days 4 and 5. When combined with 60 mg/kg/day of nikethamide, the action of phenobarbital was significantly increased on days 4 and 5, but the infants still appeared sleepy. Administration of the same dose of phenobarbital in combination with 100 mg/kg/day nikethamide decreased serum bilirubin concentrations even further, and the infants showed no signs of sedation. While phenobarbital alone decreased serum bilirubin to 2/3 of its initial level on day 5, phenobarbital + 100 mg/kg/day nikethamide reduced serum bilirubin to 1/5 of the initial level. Preliminary investigations on premature newborns indicate that exchange transfusions are no longer necessary when phenobarbital and nikethamide are administered.

7724 DIAGNOSIS OF GILBERT'S SYNDROME: ROLE OF REDUCED CALORIC INTAKE TEST. *(E.)* Owens, D.; Sherlock, S. (Roy. Free Hosp., London, England). *Br. Med. J.* 3(5880):559-563, 1973.

Reduction to 400 calories/day for 72 hr caused significant increases in the plasma bilirubin concentration in 10 patients with Gilbert's syndrome and in 12 normal subjects. In normal subjects the mean concentration rose from 0.5-0.8 mg/100 ml after 48 hr, while in the Gilbert's syndrome patients the mean concentration rose from 1.8-3.5 mg/100 ml within 24 hr. These increases were due to increased unconjugated pigment. There was no significant increase in the bilirubin concentration in 12 patients with liver disease or in 3 with hemolytic anemia. The increase in unconjugated bilirubin was significantly greater in Gilbert's syndrome (1.5-3.4 mg/100 ml) than in normals (0.3-0.5 mg/100 ml) but only when the initial bilirubin concentration was raised. In Gilbert's syndrome the increase usually exceeded 100% within 24 hr of reducing the caloric intake. It is suggested that this increase may be due to a decrease, similar to that observed in rats starved for 72 hr, in hepatic bilirubin uridine diphosphate glucuronyl transferase activity. The effect of a 400 caloric diet for 24 hr on the unconjugated bilirubin level may distinguish Gilbert's syndrome from other causes of unconjugated hyperbilirubinemia.

7725 STUDIES ON THE NEPHROTOXIC EFFECT OF BILIRUBIN ON URINARY ENZYME EXCRETION IN NEWBORNS. *(Ger.)* Gekle, D.; Kuhner, U. (Pediatric Clin., Univ. Wurzburg, Germany). *Monatsschr. Kinderheilkd.* 120(8):304-307, 1972.

Serum bilirubin and urinary LDH, leucine arylamidase (LAA), and alkaline phosphatase (AP) activities were monitored for several days in 9 infants, aged 2-18 days, with hyperbilirubinemia (serum bilirubin levels up to 19.4 mg/100 ml) and in 3 controls. Urinary enzyme activities were higher in infants with hyperbilirubinemia than in controls, e.g., LDH activities never exceeded 2.3 mU/ml in controls but increased to as high as 27 mU/ml in hyperbilirubinemia. Simultaneous decreases occurred in serum bilirubin levels and urinary LDH activities. This correlation was not as close for LAA and AP: urinary LAA activities increased for a short time before they decreased in 5 infants, and urinary AP activities followed a similar pattern. The reason for this time lag is not clear. A very large increase in urinary LDH activity occurred in an infant who was given colistin, a nephrotoxic drug. It might be anticipated that the nephrotoxic effect of lipid-soluble bilirubin could be explained by damage produced in cell membranes; bilirubin would then pass into cells in the renal tubules, liberating enzymes which are then excreted in the urine. If this were true, AP, the most important enzyme in the brush border, should be found in large quantities in the urine. However, urinary AP activities exceeded 3.5 mU/ml in only 4 of 33 determinations made on infants with hyperbilirubenimia; this value is only in the upper normal range. It is considered more likely that bilirubin damages mitochondrial membranes and interfer with uncoupling of oxidative phosphorylation. It is recommended that urinary enzyme determinations be used to test the nephrotoxicity of drugs in newborns and young infants.

7726 ORAL PHENOBARBITAL IN THE PREVENTION OF HYPERBILIRUBINEMIA IN THE PREMATURE NEONATE. *(Sp.)* Diaz de Castillo, E.; Aguilar Vivas, J. I.; Abdo Bassol, F.; Martinez-Garza, V. (Inst. Mex. Seguro Soc.). *Rev. Med.* 11(1):17-23, 1972.

A study was made to determine whether phenobarbital could be given p.o., rather than i.m., to prevent hyperbilirubinemia in premature newborns so that the inconveniences of i.m. administration could be avoided. Phenobarbital (5 mg/kg/day p.o.) was administered to 54 infants weighing 2500 g or less at birth; 35 premature infants who did not receive treatment served as controls. Any infant with Rh or ABO incompatibility or any sign of disease was not included in this study. An analysis of indirect bilirubin values showed that these were significantly lower in infants given phenobarbital than in untreated controls. Values of indirect bilirubin reached 10.1 mg/100 ml or higher in 50% of the untreated controls and in 12% of those treated with phenobarbital; 15% of the untreated group but only 3% of the treated group had indirect bilirubin values of 15.0 mg/100 ml or higher. It is recommended that phenobarbital be given p.o. to premature infants to reduce the possibility of bilirubin encephalopathy.

7727 EXCRETION OF BILE ACIDS IN EXTRAHEPATIC BILIARY ATRESIA AND INTRAHEPATIC CHOLESTASIS OF INFANCY. *(E.)* Norman, A.; Strandvik, B. (St. Goran's Children's Hosp., Stockholm, Sweden). *Acta Paediatr. Scand.* 62:253-263, 1973.

A study was made of 24 infants (16 boys and 8 girls) with obstructive jaundice. Extrahepatic biliary atresia (BA) was found in 5 infants and intrahepatic cholestasis of infancy (IHC) in the other 19. The mean daily values of cholic and chenodeoxycholic acids in urine and the ratio of cholic to chenodeoxycholic acid were similar in both groups. After the injection of isotopic cholic acid, most of the isotope was recovered in the urine in all cases. The fecal excretion of the isotope was less than 3% of the injected amount in infants with BA and in 11 of the 19 infants with IHC. In the remaining 8 infants with IHC, 4-25% of the injected isotope was excreted in the feces. In all cases, the urine specimen at 24 hr after isotope injection still contained small amounts of unconjugated labeled cholic acid. This did not occur 48 hr after injection. No differences were noted between the 2 groups with regard to the percentage labeled glycine conjugates of total excreted urinary conjugates, or with regard to half-life and pool size of cholic acid. No differences in bile acid metabolism were seen between infants with congenital cytomegalovirus infection, decreased serum concentrations of α_1-antitrypsin, and the other patients.

7728 UNBOUND BILIRUBIN IN ICTERIC NEWBORNS. *(E.)* Nakamura, H.; Lardinois, R. (Port-Royal Hosp., Univ. Paris, France). *Biol. Neonate* 21(5):400-417, 1972.

7729 PRESENTLY RECOGNIZED FORMS OF INHERITED JAUNDICE IN INFANCY. A SUMMARY AND REVIEW. *(E.)* Colon, A. R.; Sandberg, D. H. (Univ. Miami, Sch. Med., Fla.). *Clin. Pediatr.* 12(6):326-332, 1973.

7730 BILIRUBIN CLEARANCE IN HEALTHY AND PATHOLOGICAL NEWBORNS. Heringova, A.; Jirsova, V.; Polacek, K. (Inst. Care Mother Child, Prague, Czechoslovakia). *Biol. Neonate* 21:303-308, 1972.

7731 TREATMENT OF CHOLESTASIS WITH PHENOBARBITAL. *(Ger.)* Stiehl, A. (Med. Clin., Univ. Heidelberg, Germany). *Z. Gastroenterol.* 10(8):605-608, 1972.

See also, 6463, 6471, 6474, 6486, 6505, 6873, 7224.

LIVER AND BILIARY TRACT

Nonviral Hepatitis and Hepatic Injury

7732 JAUNDICE FOLLOWING FLUROXENE ANESTHESIA. *(E.)* Harris, J. A.; Cromwell, T. H. (Naval Hosp., San Diego, Calif.). *Anesthesiology* 37(4):462-463, 1972.

A 39-yr-old Caucasian male was admitted for elective thoracotomy for biopsy of a mass discovered on x-ray. The patient was healthy and all tests were normal. Fluroxene (about 2%) was used to help maintain the anesthesia during the 1.5 hr operation. On the 4th postoperative day, serosanguineous wound drainage was seen. Oxacillin sodium therapy was started. Visible jaundice, spiking fever, and a pulmonary infiltrate in the right lobe had developed by day 5. Laboratory tests showed bilirubin, 4 mg/100 ml; alkaline phosphatase, 260 mU/ml; SGOT, 445 mU/ml. Oxacillin sodium therapy aided in healing the infected wound. By the 12th day, laboratory test functions had returned to normal. It is suggested that fluroxene causes hepatic damage similar to that described for halothane, as both agents have similar biodegradation products.

7733 THE CHLORAMPHENICOL-HEPATITIS-APLASTIC ANAEMIA SYNDROME. *(E.)* Hodgkinson, R. (Albert Einstein Sch. Med., New York, N.Y.). *Med. J. Aust.* 60(19):939-940, 1973.

Chloramphenicol (from 8 - 62 gm) was given to 5 patients (3 females and 2 males, aged 4 - 63 yr) for treatment of respiratory infections, including recurrent bronchitis (3); whooping cough (1); and urinary infection (1). The length of treatment ranged from 8 days to 2½ months. Jaundice developed from 3 to 6 weeks after treatment in 3 cases, and during the end of the treatment in the other 2. This was commonly accompanied by anorexia, nausea, and depression. At the time of the jaundice, blood counts revealed no hematological abnormality. Serum bilirubin ranged from 7 to 18 mg/100 ml; SGPT from 250- to 1400 IU. As the jaundice was clearing, or after it had cleared, problems with purpura, spontaneous bruising, hemorrhaging, ecchymoses, and epistaxis developed. Necropsy revealed hemorrhage into various organs and complete aplasia of the marrow. In 1 case the liver was enlarged with areas of necrosis, fibrosis, and active regeneration. In another, the liver showed Laennec's cirrhosis. It is noted that this syndrome is almost identical to that occurring after trinitrotoluene administration.

7734 HEPATITIS INDUCED BY LAXATIVES: A CONTRIBUTION TO OXYPHENISATIN JAUNDICE. *(Ger.)* Dahinden, U.; Filippini, L.; Rondez, R. (Cantonal Hosp., Lucerne, Switzerland). *Schweiz. Med. Wochenschr.* 103(27):960-964, 1973.

A 56-yr-old woman, hospitalized with jaundice and increased serum bilirubin, alkaline phosphatase, and SGOT values, improved rapidly without any treatment and was discharged with a diagnosis of acute hepatitis. Recurrent jaundice, which developed soon after her discharge, responded briefly to corticosteroids, but the patient had to be hospitalized again because of a deterioration in her general condition. A liver biopsy at this time showed marked periportal inflammation and fibrosis, the presence of many Councilman bodies in the hepatic parenchyma, many vacuoles and some bile in the cytoplasm of hepatocytes, a moderate increase in the number of Kupffer cells with occasional deposits of pigment, and interlobular bile ducts with an irregular and vacuolized epithelium. The patient again recovered after 2 weeks and was discharged with a diagnosis of protracted hepatitis. A second recurrence of jaundice occurred 2 weeks later, and the patient developed spider nevi. Biopsy findings during this third hospitalization were similar to those described above, but Councilman bodies had been replaced by areas of lytic necrosis, Kupffer cell proliferation was more pronounced, and more bile thrombi were present. The findings were compatible with chronic recurrent hepatitis with marked cholestasis. On questioning, the patient admitted that she had taken a laxative containing oxyphenisatin acetate every day for 2 yr before her hospitalization and in the intervals between hospital stays. The patient again recovered after 2 weeks, and was discharged with a warning not to take any laxatives containing oxyphenisatin. All findings were normal at a follow-up examination made 5 months later. With the exception of noncharacteristic abdominal pain and spider nevi, the clinical and laboratory findings observed for this patient are characteristic for oxyphenisatin hepatitis. It is recommended that all patients with hepatitis be questioned about their use of laxatives. Since other effective laxatives are readily available, oxyphenisatin-containing laxatives should be taken off the market.

7735 PSORIASIS-LIVER-METHOTREXATE INTERACTIONS. *(E.)* Weinstein, G.; Roenigk, H.; Maibach, H.; Cosmides, J.; Halprin, K.; Millard, M. (Univ. Miami Sch. Med., Fla.). *Arch. Dermatol.* 108(1): 36-42, 1973.

A study was made of 742 liver biopsies from 550 patients (about 314 males and 233 females, mean age of 46.9 yr). Some of the bipsies were obtained before, and others after, methotrexate therapy. Mean skin surface area covered by psoriasis was 61.5%. Hepatomegaly was noted in 10.6% of the patients before receiving methotrexate therapy and in 6.9% after receiving the drug. The first post-methotrexate liver biopsy occurred on the average of 2.8 yr after starting therapy. Of the 372 patients biopsied after drug therapy, 72 had used the drug for 5 or more years, the longest was 11 years. Neither sex, age, nor extent of psoriasis had any correlation with abnormal histologic liver changes. Increased alcohol intake was significantly associated with fatty metamorphosis in pre-drug patients. In post-drug patients, increased alcohol correlated with the presence of periportal inflammation, fibrosis, and cirrhosis. Obesity was associated with fatty metamorphosis of the liver in both pre- and post-methotrexate patients. Past histories of systemic administration of corticosteroid were not associated with liver damage. Diabetes was associated with abnormal histologic findings in both pre- and post-drug groups. The presence of liver damage was significantly associated with increasing cumulative doses of methotrexate and daily oral dosage schedule of drug administration *vs.* weekly oral, weekly i.m. or i.v., or divided weekly oral schedules. Duration of therapy was not significant in the pathologic changes of the liver. Of 247 patients with biopsy proven fibrosis or cirrhosis, 88 had no abnormalities in history, physical findings, or liver function tests, suggesting that there are no reliable clinical or biochemical indicators of hepatic fibrosis or cirrhosis.

7736 HEPATIC TOLERANCE OF ANTITUBERCULAR DRUGS INCLUDING RIFAMPICIN: STUDY OF 214 CASES.

(Fr.) Decroix, G.; Pujet, J. C. (St. Antoine Hosp., Paris, France). *Sem. Hop. Paris* 49(30):2219-2224, 1973.

Rifampicin (600 mg/day) and isoniazid (300-600 mg/day), associated with either streptomycin or ethambutol, were administered to 173 patients with tuberculosis; 41 patients received all these tuberculostatics but the rifampicin. A group of 124 hospitalized patients with no evidence of tuberculosis served as controls. Within 10-90 days after institution of treatment, serum transaminase levels increased in 40 of the 173 patients (23%) given rifampicin, but in only 3 of 41 patients (7.5%) given tuberculostatics without rifampicin and in 5 of the 124 nontubercular controls (4%). Jaundice developed in 17 patients treated with tuberculostatics and in none of the nontubercular controls. Of these 17 patients, 7 were Australia-antigen positive and 5 were Australia antigen negative; Australia antigen determinations were not performed in the remaining 5 cases. Transaminase values were significantly higher in the 7 Australia antigen-positive patients, suggesting that rifampicin could lower resistance to viral hepatitis. Jaundice was more prevalent among alcoholics (11 cases) than among nonalcoholics (6 cases) and among patients given rifampicin (16 of 17 cases). Although the jaundice lasted for only 8-30 days in most patients, it persisted for 4 and 5 months, resp. in 2 patients. Death could not be attributed to hepatitis alone in any of the 3 patients who died. Other contributing factors were (1) aspergillosis; (2) esophageal cancer and tuberculosis; and (3) cirrhosis and multiple bilateral pulmonary embolisms secondary to a venous thrombosis in the left leg. Rifampicin was discontinued after the onset of jaundice in 9 of the remaining 14 patients and was continued without any difficulty in 3 cases. A recurrence developed in 1 patient after rifampicin was reinstituted, but 2 patients had recurrences several months later without being given any more of the drug. One patient treated with rifampicin, isoniazid, and p-aminosalicylic acid developed moderate jaundice with unconjugated bilirubin. The jaundice regressed and transaminase activities normalized within a few days after the dose of rifampicin was reduced to 900 mg twice a week. To prevent jaundice from developing in patients treated with rifampicin and isoniazid, therapy should be begun with small doses of both drugs, particularly in patients with impaired liver function. It is also possible to combine rifampicin with ethambutol and/or streptomycin, rather than with isoniazide.

7737 PELIOSIS HEPATIS: POSSIBLE ETIOLOGICAL ROLE OF DRUGS.

(Fr.) Delage, C.; Lagace, R. (Hotel Dieu, Quebec, Canada). *Union Med. Can.* 102(9):1888-1893, 1973.

A 65-yr old man with subacute myeloid leukemia obtained a partial remission lasting 18 months with hydroxyurea (500-1500 mg/day for 6 weeks) and a single dose of radiation (300 rads). The patient was hospitalized again for a myeloblastic transformation of chronic myeloid leukemia. Despite treatment with vincristine sulfate, prednisone, and allopurinol during the last 12 days of hospitalization, the patient died 45 days after admission. In addition to leukemic infiltrates in all organs, autopsy showed that the liver contained many small, blood-filled cavities, 2-5 mm in diameter. These cavities occurred randomly in the liver and, under the light microscope, did not have a clear-cut endothelial lining. The absence of this lining and the absence of focal necrosis and cholestasis make it impossible to classify this case of peliosis hepatis among the parenchymal or phlebectatic forms. Although no cause-effect relation between peliosis hepatis and hydroxyurea could be demonstrated, this drug is considered a possible cause of peliosis hepatis since it was administered for a relatively long period (6 weeks) 18 months before the patient died.

7738 HEPATIC GRANULOMAS.

(Fr.) Antille, J. C.; Portmann, B.; Mach, R. S. (Cantonal Hosp.,

neva, Switzerland). *Ann. Med. Interne (Paris)* 4(6/7):493-499, 1973.

a 5-yr period, hepatic granulomas were found in of 2324 punch biopsies of the liver (3.30%). ong patients with fevers of unknown origin, diagses were established by liver biopsy for miliary berculosis of the liver (24 cases), brucellosis cases), Hodgkin's disease (7 cases), rickettsiosis case), and periarteritis nodosa (3 cases). Liver anulomas were also used to confirm the diagnosis sarcoidosis in 18 cases, schistosomiasis in 3 ses, and secondary syphilis in 1 case. In dition, liver granulomas were found in 1 patient th typhoid fever and in 1 patient with Crohn's sease. The etiology of hepatic granulomas could t be established in 12 of the 79 patients (16%). lustrative case reports are presented.

39 LYMPHOCYTE TRANSFORMATION. ABSENCE OF INCREASED RESPONSES IN ALLEGED HALOANE JAUNDICE. *(E.)* Walton, B.; Dumonde, D. C.; lliams, C.; Jones, D.; Strunin, J. M.; Layton, M.; Strunin, L.; Simpson, R. (London Hosp., gland). *J. A. M. A.* 225(5):494-498, 1973.

vitro tests for cell-mediated immunity were concted in a group of 10 patients and 5 physicians ose histories suggested the possibility of hypernsitivity to halothane. Lymphocytes from these bjects were tested for transformation in the esence of phytohemagglutinin (1, 10, and 100 /ml), halothane (16 and 32 μg/ml), methoxyurane (23 and 46 μg/ml), diethyl ether (220 and 0 μg/ml), and trichloroethylene (22.5 and 45 μg/ml). e results were not significantly different from e results in a group of normal controls. These ndings, therefore, fail to confirm previously ported work, which claimed that positive lymphote transformation was demonstrated in 10 of 15 tients with alleged halothane hepatitis.

40 ISONIAZID HEPATITIS. *(E.)* Maddrey, W. C.; Boitnott, J. K. (Johns Hopkins sp., Baltimore, Md.). *Ann. Intern. Med.* 79(1): -12, 1973.

patitis secondary to isoniazid (300 mg/day) given a chemoprophylactic drug for tuberculosis was served in 14 patients (3 males and 11 females, ed 19-66 yr) over 5 yr. Of these patients, died with fulminant hepatic failure, and 8 of e 11 surviving had bridging or multilobular neosis, or both, on liver biopsy. Serum bilirubin nged from 2.3 to 27.2 mg/100 ml; SGOT from 26- 00 milli-IU; and alkaline phosphatase from 25.1 319 milli-IU. Rechallenge with isoniazid led an accelerated recurrence of severe hepatitis 2 patients and abnormal serum transaminases thin 2 days in a third. A prodromal period aracterized by fatigue, weakness, anorexia, and laise was noted in all patients before the appearance of jaundice. The duration of the symptomatic interval during which isoniazid was continued was longer (mean, 4.6 weeks) in the patients with bridging or multilobular necrosis than in those with only diffuse hepatitis (mean, 2.2 weeks), suggesting that once symptoms appear continued use of the drug causes more severe liver damage. Each of the 3 deaths occurred in females who continued to take the drug 1-8 weeks after the onset of symptoms (2), or in whom the drug was reinstituted during the initial bout of hepatitis (1). These observations support the need for close medical follow-up of patients on isoniazid therapy, with immediate investigation of symptoms that suggest an adverse reaction.

7741 ULTRASTRUCTURAL PATHOLOGY OF A CASE OF HALOTHANE HEPATITIS. *(E.)* Schatzki, P. F.; Kay, S.; McGavic, J. D. (McGuire VA Hosp., Richmond, Va.). *Am. J. Dig. Dis.* 18(10):905-911, 1973.

A 26-yr-old male with hepatitis induced by repeated sniffing of halothane was examined. Light microscopy showed necrosis and ballooning of liver cells in central areas without nuclear unrest and with minimal inflammatory activity. Electron microscopy revealed cell shrinkage with dark-staining liver cells, myelin-like figures, enlargement of the intercellular space, and intercellular villus formation. Large intracellular areas free of organelles were present in the balloon cells. Mitochondria appeared quite well preserved, even in areas adjacent to intracellular ballooning. Some cells contained bundles of fibrillar material. The pattern appears to be largely nonspecific cellular injury and necrosis.

7742 CURRENT PROBLEMS AND ATTITUDE TO THE PROBLEM OF CHRONIC LIVER DAMAGE PRODUCED BY HALOTHANE IN ANESTHESIA PERSONNEL. *(Ger.)* Schulze, H. H.; Kastner, D. (Konigs Wusterhausen Reg. Hosp., Germany). *Anaesthesist* 22(2):47-50, 1973.

Gas chromatographic measurements showed that the mean concentration of halothane in the air of an operating room was 13-15 ppm when the halothane evaporator was operated at 1.5% by volume. Halothane concentrations in the blood of anesthetists working for 4 hr/day in an operating room where halothane was being used ranged from 0.008 to 0.0165 μliter/100 ml. Surgeons had only traces of halothane in their blood. Of 3 nurses exposed to halothane, 1 had an abortion in the 6th month of pregnancy and 1 delivered prematurely.

7743 ANTIHEPATOTOXIC ACTIVITY OF PARENTERALLY APPLIED SILYMARINE IN GALACTOSAMINE HEPATITIS OF THE RAT. *(Ger.)* Schriewer, H.; Rauen, H. M. (Physiol Chem. Inst., Univ. Munster/Westfalen, Germany). *Arzneim. Forsch.* 23(1a):159, 1973.

7744 HALOTHANE ANESTHESIA AND HEPATITIS IN A HIGH-RISK POPULATION. *(E.)* Greene, N. M. (Yale Univ. Sch. Med., New Haven, Conn.). *N. Engl. J. Med.* 289(6):304-307, 1973.

7745 HAEMOSTASIS DURING GALACTOSAMINE HEPATITIS. *(Ger.)* Krause, W.; Hey, D.; Leinweber, B. (Med. Clin., Justus Liebig Univ., Giessen, Germany). *Klin. Wochenschr.* 50(7):386-387, 1972.

7746 LIVER CELL ULTRASTRUCTURE IN ACUTE PERITONEAL POISONING WITH BENZENE. *(Pol.)* Jonek, J.; Kaminski, M.; Kaminska, O.; Glanc, A.; Bruszeczka, B. (Silesian Acad. Med., Katowice, Poland). *Med. Pracy* 24(2):159, 1973.

7747 HEPATIC TRAUMA: 5 PATIENTS WHO HAD TO UNDERGO MAJOR EMERGENCY HEPATIC RESECTION. *(Fr.)* Atlas, H.; Allard, M.; Marcade, J. P. (Sacre Coeur Hosp., Canada). *Union Med. Can.* 102(6):1291-1299, 1973.

7748 GONOCOCCAL PERIHEPATITIS AND GONOCOCCAEMIA. PRESENTATION OF A CASE WITH CUTANEOUS MANIFESTATION. *(E.)* Lassus, A.; Kousa, M. (Univ. Ctr. Hosp., Helsinki, Finland). *Br. J. Vener. Dis.* 49(1):48-49, 1973.

7749 ANATOMICAL AND FUNCTIONAL DAMAGE TO THE LIVER IN CALCULOSIS OF THE BILIARY TRACT. *(E.)* Russo, A.; Rasa, G.; Ippolito, O.; Banna, P.; Di Benedetto, L.; Sanfilippo, G. (Inst. Gen. Clin. Surg. Surg. Therap., Univ. Catania, Italy). *Chir. Gastroenterol.* 6(4):335-346, 1972.

See also, 6450, 6674, 6823, 7708.

LIVER AND BILIARY TRACT

Acute Viral Hepatitis

7750 CHANGES IN "PLASMA RENNIN ACTIVITY" DURING ACUTE VIRAL HEPATITIS. *(It.)* Antonello, A.; Favaro, S.; Baggio, B.; Cadrobbi, P.; Todesco, S.; Borsatti, A.; Naccarato, R. (Inst. Special Med. Pathol. Clin. Methodol., Univ. Padua, Italy). *Boll. Soc. Ital. Biol. Sper.* 48(12):307-309, 1973.

By using the radioimmunological test for angiotensin I, plasma renin activity was determined for 11 patients (6 males and 5 females, aged 12-43 years) with the acute stage of viral hepatitis. Plasma renin activity averaged 10.06 ± 5.22 ng/ml/hr in patients with hepatitis and 1.13 ± 0.57 ng/ml/hr in normal subjects. The differences in plasma renin activity between these 2 groups is highly significant. The increase in plasma renin activity in acute viral hepatitis is probably caused by failure of the liver to catabolize this enzyme due to a decrease in the affinity of liver cells for renin. It is unlikely that increased plasma renin activity is caused by increases in angiotensinogen since this precursor of angiotensin tends to decrease in other liver diseases.

7751 HEPATITIS-ASSOCIATED ANTIGEN, SUBTYPES D AND Y. AN EPIDEMIOLOGICAL AND CLINICAL EVALUATION. *(E.)* Skinhoj, P. (Bispebjerg Hosp., Copenhagen, Denmark). *Scand. J. Infect. Dis.* 5(2):85-89, 1973.

The distribution of hepatitis associated antigen (HAA) subtypes D and Y was investigated in 3 different geographical areas in 466 sera from different population groups and from patients with acute and chronic hepatitis. The D subtype predominated (94%) in all groups of Danes except for drug addicts in whom the Y subtype occurred in 84%. Subtype D also predominated in those individuals studied in an institution for the mentally retarded. In Greenlanders, only the D subtype was found on the east coast, whereas only the Y subtype occurred on the northwest coast. On the southwest coast the 2 subtypes occurred in equal proportions independent of a diagnosis of infectious hepatitis, suggesting that the occurrence of HAA is unrelated to the hepatitis outbreak. Only the Y subtype was found in patients and blood donors of southeast European or

Arabic origin. No differences were found in the distribution of subtypes D and Y among patients with various liver diseases and healthy carriers. The difference in subtype distribution in drug addicts compared with other Danes might imply that the Y subtype is more easily transmitted by the parenteral route. However, this does not appear to be the case in Greenlanders and individuals of Eastern Mediterranean origin in whom no parenteral exposure was suspected. It is suggested that Danish drug addicts may have been infected from sources of Eastern Mediterranean origin since these countries are frequently visited by drug addicts. However, more investigation of the epidemiology of HAA subtypes is needed before any definitive conclusion can be reached.

7752 ARTHRITIS AND HB Ag-POSITIVE HEPATITIS. *(E.)* McCarty, D. J.; Ormiste, V. (Dept. Med., Univ. Chicago, Ill.). *Arch. Intern. Med.* 132(2):264-268, 1973.

In 3 patients with Australia antigen (HB Ag)-positive hepatitis, arthritis was observed throughout the entire course of the disease. Several features relative to the natural history of this syndrome emerged. First, the arthritis resolved gradually during the period of hepatitis, overlapping, rather than preceding it. Persistent low-grade arthritic symptoms which were present in 1 patient for more than 7 months were associated with mild liver function abnormalities and HB Ag-positivity in his serum. This patient was anicteric and, except for arthritis, would never have sought medical attention. Second, only 1 of 3 patients showed a decreased serum hemolytic complement level despite repeated testing. Third, HB Ag was detected in a joint fluid. Concomitant total hemolytic complement and total protein determinations on this fluid and serum showed that joint fluid hemolytic complement levels were depressed. Fourth, the arthritis is clinically distinct from rheumatoid arthritis although both syndromes share certain features. Fifth, the concept of an arthritogenic strain of the infectious agent is supported as 2 of these patients, 1 of their colleagues, and the patient from whom they contracted hepatitis all had arthritis.

7753 CYTOGENETICAL FINDINGS IN CHILDREN BORN TO CARRIERS OF HEPATITIS-ASSOCIATED ANTIGEN. *(E.)* Mikkelsen, M.; Skinhoj, P.; Olesen, H. (John F. Kennedy Inst., Glostrup, Denmark). *Acta Pathol. Microbiol. Scand.* [*B*] 81(2):207-218, 1973.

Chromosome studies were made on 50 newborn infants (25 boys and 25 girls) born to healthy carriers of hepatitis associated antigen (HAA). HAA was not detected in cord blood from the infants, and all infants remained healthy and HAA-negative for 4-12 months after birth. No syndromes associated with chromosome abnormalities were observed. The number of abnormal cells was significantly higher in infants born to HAA-positive mothers (14.71%) than in controls (7.77%). This difference was largely due to the significantly larger number of amodal cells in infants born to HAA carriers. Chromosomes from the D and G groups were lost significantly more often in both infants born to HAA carriers and controls. Cells with rings and dicentrics were found in both groups, but the number of culture failures was significantly greater among infants born to HAA carriers. These findings suggest that infection with viral hepatitis occurred early in pregnancy, even though no HAA could be detected in the cord blood. It is also possible that the virus may have induced a tolerant carrier state with an undetectable serum concentration of HAA. Since it is not known whether such infections become important later in life, these infants will be followed to determine whether infection with serum hepatitis virus during early stages of embryogenesis has any effects, especially on the development of malignancies such as leukemia, later in life.

7754 HEPATITIS B ANTIGEN (HB-Ag, AUSTRALIA ANTIGEN) IN MIXED SALIVA OF PATIENTS WITH HB ANTIGENEMIA. *(E.)* Kistler, G. S.; Sonnabend, W.; Krech, U. (Dept. Anat., Univ. Zurich, Switzerland). *Pathol. Microbiol.* 39(5):313-318, 1973.

Hepatitis B antigen (HB Ag) was detected by immunodiffusion in mixed saliva obtained from 2 of 4 patients with acute hepatitis B, 1 of 3 with chronic hepatitis, 2 of 3 with cirrhosis, and in both of 2 patients with kidney transplants. All patients had HB Ag-positive sera. Electron microscopy of the precipitin lines of the immunodiffusion preparation showed variable-sized complexes of HB-Ag-like particles, measuring about 20-25 nm in diameter, with some larger ones having diameters of 40-50 nm. The particles were connected by minute, short filaments. In 2 preparations the particles were intermingled with globules of variable size, presumably agarose. The larger particles did not have the inner component typical for Dane particles. However, it is assumed that they may be complete virus particles and that the saliva must be considered potentially infectious. It is not certain whether the negative results in 5 of these 12 patients are due to lack of methodological sensitivity or to differences caused by various phases of disease development. No positively reacting cells were detected in preparations made of salivary WBC obtained from patients with HB Ag-positive sera. It is not yet known whether HB Ag (and possibly complete virus) is (1) carried by blood WBC to the oral cavity, (2) is transmitted from the blood into salivary gland secretions by an unknown pathway, or (3) is produced within epithelial cells of the salivary glands.

7755 ROLE OF MOSQUITOES IN TRANSMISSION OF HEPATITIS B ANTIGEN. *(E.)* Byrom, N. A.; Davidson, G.; Draper, C. C.; Zuckerman, A. J. (London Sch. Hyg. Trop. Med., England). *J. Infect. Dis.* 128(2):259-260, 1973.

Six species of mosquitos (*Anopheles albimanus, A. gambiae* [2 strains], *A. stephensi, Aedes aegypti, Mansonia uniformis*, and *Culex pipiens fatigans*) were fed artificially on blood from 2 healthy carriers of viral hepatitis. Feeding results were independent of the subtype (*ay* or *ad*) of antigen present in the blood. Addition of a trace of ATP markedly enhanced feeding activity. A sensitive radioimmunoassay technique showed that all of the ingested antigen disappeared in parallel with digestion of the blood meal; within 24 hr after feeding no antigen was detected. There was no evidence that hepatitis B antigen replicated. Although these findings indicate that none of the 6 species of mosquitoes investigated act as biological vectors of hepatitis B antigen, they do not rule out the possibility that the antigen might be transmitted mechanically from the mouth parts of mosquitoes. The high prevalence of hepatitis B antigen carriers in the tropics may be due to such a mode of transmission.

7756 A POSSIBLE RELATIONSHIP BETWEEN PERSISTENT HEPATITIS B ANTIGENAEMIA AND RENAL DISEASE IN SOUTHERN AFRICAN BANTU. *(E.)* Vos, G. H.; Grobbelaar, B. G.; Milner, L. V. (Natal Inst. Immunol., Durban, South Africa). *S. Afr. Med. J.* 47(21):911-912, 1973.

Blood samples from 182 South African Bantu patients with renal disease were examined for hepatitis B antigen (HB Ag) with inhibition cross-over electrophoresis. Studies were also made of 245 apparently healthy blood donors with persistent HB antigenemia, and 141 blood donors who were negative for HB Ag. Depressed serum complement C3 levels were just as common among chronic carriers of HB Ag as among HB Ag-positive Bantu patients. The mean serum complement C3 value was 102 mg/100 ml among known carriers of HB antigen and 141 mg/100 ml among HB Ag-negative blood donors lacking this viral antigen. However, the standard deviation of the C3 values was similar in both groups, indicating the difference in C3 values was due to a shift in its quantitative distribution. A much wider range of complement C3 levels, both above and below the expected range for normal individuals, was found in patients with renal disease. It is suggested that the variable distribution of C3 values among persistent HB Ag carriers may reflect immune activation and utilization of the complement sequence by HB antigen-antibody complexes. In 182 glomerulonephritis patients, the incidence of HB Ag carriers was 20.3% as compared to 9.8% in healthy blood donors. The difference in distribution of HB Ag between the 2 groups suggests a relation between the HB Ag carrier state and the pathogenesis of renal disease. The fact that many HB Ag carriers had reduced serum complement C3 levels supports the theory that renal pathology may be due to deposition of immune complexes on the glomerular basement membrane.

7757 LIMITATIONS OF SOLID-PHASE RADIOIMMUNOASSAY FOR HB Ag IN REDUCING FREQUENCY OF POST-TRANSFUSION HEPATITIS. *(E.)* Hollinger, F. B.; Aach, R. D.; Gitnick, G. L.; Roche, J. K.; Melnick, J. L. (Baylor Coll. Med., Waco, Tex.). *N. Engl. J. Med.* 289(8):385-391, 1973.

To determine if a recently licensed radioimmunoassay (Ausria-125) would further reduce the incidence of type B hepatitis, 139 presumably susceptible recipients were prospectively studied after they had received blood negative for hepatitis B antigen by counterelectrophoresis. Icteric or anicteric hepatitis occurred in 15 cases, but only 4 could be attributed to hepatitis B. No hepatitis B occurred in 9 subjects who received radioimmunoassay-positive blood alone, and in only 1 of 10 who had received radioimmunoassay-positive and hepatitis B-antigen-positive blood. Of 120 patients who received radioimmunoassay-negative blood, only 3 developed type B hepatitis. If serologic responses alone are compared, exposure to hepatitis B or hepatitis B antigen occurred in 6 of 19 recipients of radioimmunoassay-positive blood. These results do not support universal compulsory implementation of the Ausria immunoassay for screening blood donors to reduce the risk of hepatitis.

7758 HEPATITIS: INTRAHEPATIC EXPRESSION OF AU ANTIGEN AND IMMUNE COMPLEXES IN LIVER TISSUE. *(E.)* Kater, L.; Van Gorp, L. H. M.; Borst Eilers, E. (St. Antonius Hosp., Utrecht, Netherlands). *Vox Sang.* [*Supp.*] 24:27-32, 1973.

Patients with various liver disorders were studied for the presence of (Au) antigen in their blood, as well as for the presence of Au antigen, immuno o lins, and complement in their liver. In 18 patients,

Patients with various liver disorders were studied for the presence of Australia (Au) antigen in their blood, as well as for the presence of Au antigen, immunoglobulins, and complement in their liver. In 18 patients, diagnosed as acute infectious hepatitis (2), acute serum hepatitis (12), healed serum hepatitis (1), chronic active hepatitis (1), chronic hepatitis (1), and chronic aggressive hepatitis (1), Au antigen was observed in the serum. In all these, Au antigen was also found in the liver. In both Au-positive and Au-negative hepatitis, granular deposition of IgG and complement was noted in the liver along vessel walls and sinusoids. These findings suggest that immune complexes are involved in the pathogenesis of viral hepatitis.

7759 A URINARY SUBSTANCE IN PATIENTS WITH ACUTE TYPE-B HEPATITIS AND THEIR HOUSEHOLD CONTACTS. *(E.)* Heathcote, J.; Tsianides, A.; Sherlock, S. (Roy. Free Hosp., London, England). *Lancet* (7829):593-595, 1973.

Some concentrated urine samples collected from patients with acute type-B hepatitis and their household contacts gave a positive complement-fixation test with antisera to the hepatitis-B antigen

(HBAg). But typical HBAg particles were not seen in these urine samples. Of 52 HBAg-positive hepatitis patients studied at hospitalization, only 5 had a positive urine test. However, when 20 of these patients and 6 other similar patients (whose urine was not tested in the acute phase of their illness) were followed monthly for 6 months, 18 had a positive urine test on at least one occasion. Monthly tests for a 6 month period were made on 71 household contacts of these 26 patients; 34 had a positive urine test on at least one occasion, although these contacts had no evidence of acute hepatitis. Significantly fewer positive urine samples were obtained from control households. These results suggest that whatever the urinary substance is which gives a positive complement fixation test with HBAg antisera, it seems related to exposure to HBAg.

7760 AUSTRALIA ANTIGEN: PERSISTENCE OF IMMUNOLOGICAL MARKERS (d, y, w) IN ANTIGEN CARRIERS. *(E.)* Mazzur, S.; Blumberg, B. S. (Inst. Cancer Res., Philadelphia, Pa.). *Infect. Immun.* 8(2):178-181, 1973.

Sequential blood samples containing Australia antigen from 31 chronic carriers were typed for determinants d, y, and w. The subjects included asymptomatic carriers from Rongelap Atoll in the Marshall Islands (7), Down's syndrome patients (12), and patients receiving renal hemodialysis (12, 4 of whom had acute viral hepatitis). The period of time between blood samples ranged from 3 months to 11 yr. In no case did the subtype change in any individual. Therefore, it seems that Australia antigen subtypes are stable epidemiological markers in both short-term infections and chronic carriers.

7761 FULMINANT HEPATITIS COMPLICATED BY PANCREATITIS. *(E.)* Wands, J. R.; Salyer, D. C.; Boitnott; J. K.; Maddrey, W. C. (Johns Hopkins Univ. Sch. Med., Baltimore, Md.). *Johns Hopkins Med. J.* 133:156-160, 1973.

A 21-yr-old man was admitted with a 1 week history of jaundice, dark urine, light stool, pruritus, and progressive nausea. Serum bilirubin, alkaline phosphatase, and amylase levels were increased. Hepatitis B antigen was present in a titer of 1:16 in the hemagglutination inhibition test. Microscopic examination of the liver tissue at autopsy revealed diffuse hepatitis, morphologically typical of viral hepatitis, with extensive bridging and multilobular necrosis. Ascites containing fat globules was present. A moderately severe acute pancreatitis, localized mainly in the tail of the pancreas with prominent peripancreatic fat necrosis, edema, focal hemorrhage, and acute inflammation were found. There was focal inspissation of secretions within the dilated intrapancreatic ducts. Postmortem records of 18 consecutive patients with fulminant hepatitis of presumed viral etiology were examined. All had histological changes compatible with viral hepatitis, and 16 had massive or submassive hepatic necrosis. Of the 18, 8 (44%) had morphological evidence of pancreatitis. Only 1 case (6%) of pancreatitis was found in a group of age- and sex-matched controls. In 3 cases the only evidence of the pancreatitis was acute interstitial inflammation. Focal parenchymal and peripancreatic fat necrosis were present in the other cases. Of these 18 patients, 6 had received corticosteroids for complicating factors, and only 2 of these 6 had pancreatitis. Similarly, the elevation of serum urea nitrogen did not appear to be related to the incidence of pancreatitis in this series. It is suggested that the diagnosis of pancreatitis be considered in any patient with fulminant hepatitis.

7762 QUANTITATIVE STUDIES OF AUSTRALIA ANTIGEN IN ACUTE AND CHRONIC HEPATITIS. EVIDENCE FOR AN INVERSE RELATIONSHIP BETWEEN CIRCULATING AU-ANTIGEN AND TRANSAMINASE VALUES IN PATIENTS WITH PROGRESSION FROM ACUTE TO CHRONIC HEPATITIS. *(E.)* Elling, P.; Nielsen, J. O.; Dietrichson, O. (Blegdam Hosp., Copenhagen, Denmark). *Vox Sang.* [*Suppl.*] 24:44-54, 1973.

Australia antigen (Au-antigen) was determined quantitatively by electrophoresis in antibody-containing gel on consecutive serum specimens from 19 patients with uncomplicated acute viral hepatitis associated with the presence of transient Au-antigen and from 9 patients with persistence of Au-antigen and histological progression from acute the chronic hepatitis. Of the 9 patients with chronic liver disease, 6 had chronic aggressive hepatitis and 3 had chronic persistent hepatitis; 7 were young drug addicts. None of the patients received corticosteroids or other immunosuppressive agents. An exponential fall in the Au-antigen concentration was observed in all patients with uncomplicated acute hepatitis, suggesting that antigen production stopped early in the disease and that the antigen was removed by a process resembling a first-order reaction. In patients with persistent antigenemia, 2 phases of the disease were observed. Initially these patients showed great variations in both the Au-antigen concentration and SGOT activity. An inverse relation between the Au-antigen concentration and SGOT values was observed. The next phase, 1-2 yr after onset of the disease, was characterized by low values of Au-antigen concentration and low SGOT activity. This pattern was observed irrespective of the histological type of chronic hepatitis. These findings provide additional evidence that damage in the liver cells of patients with Au-antigen-associated chronic hepatitis results from formation of an immune complex with Au-antigen rather than from direct cytopathogenic effects of circulatng Au-antigen.

7763 A COMPARISON OF THE FREQUENCY OF HEPATITIS-B ANTIGEN AND ANTIBODY IN HOSPITAL AND NONHOSPITAL PERSONNEL. *(E.)* Lewis, T. L.; Alter, H. J.; Chalmers, T. C.; Holland, P. V.; Purcell, R. H.; Alling, D. W.; Young, D.; Frenkel, L. D.; Lee, S. L.; Lamson, M. E. (Clin. Ctr., Natl. Inst.

Allergy Infect. Dis., Bethesda, Md.). *N. Engl. J. Med.* 289(13):647-651, 1973.

The frequency of elevated SGPT levels and hepatitis B antigen (HBAg) and antibody (HBAb) was determined in 1052 health-care personnel and in 1052 controls matched for age, sex, and socioeconomic status with no exposure to patients or blood products. HBAg was detected in 8 (0.8%) of the health-care personnel and in 4 (0.4%) of the controls; this difference is not statistically significant on testing with either counterelectrophoresis or solid-phase radioimmunoassay. The presence of HBAg in controls correlated with a history of blood transfusion; this was not true for health-care personnel. No association was found between the presence of HBAg and a history of hepatitis in either group. HBAb was significantly more frequent among health-care personnel (16%) than among controls (8.9%). Among health-care personnel, but not among controls, HBAb was more common in those with a history of hepatitis than in those with a history of hepatitis than in those who had not had hepatitis. There was no significant difference between SGPT levels in health-care personnel and in controls. The presence of HBAg and elevated SGPT values were not related to age, sex, or socioeconomic status. However, HBAb was significantly more among those belonging to lower socioeconomic groups, among women, and among subjects over 40 yr old. Of 7 HBAg-positive health workers studied, 2 were asymptomatic carriers, 2 had chronic hepatitis, 2 had acute hepatitis, and 1 had a short episode of HBAg-positivity without elevated SGPT levels. All of the 4 HBAg-positive controls studied were asymptomatic carriers. These findings suggest that there is greater reason to reject blood donors with histories of blood transfusion than those with histories of hepatitis.

7764 MORPHOLOGICAL FEATURES OF AUSTRALIA ANTIGEN IN THE COURSE OF VIRAL HEPATITIS TYPE B. *(Fr.)* Couleru, O.; Moulias, R.; German, A.; Peter; Loeper, J. (Salpetriere Hosp., Paris, France). *Ann. Med. Interne (Paris)* 124(6/7):513-519, 1973.

The role of various particles associated with Australia antigen (HAA) and their aggregates is discussed on the basis of 4000 immunological and ultrastructural studies. Spherical particles (d = 20 nm), tubular particles (20 x 40-60 nm), and a very small number of Dane particles (d = 40 nm) were found in serum from HAA-positive patients with acute viral hepatitis, while none of the particles were ever found in patients with acute viral hepatitis and antibodies to HAA. Spherical particles, alone or with a very small number of Dane particles, were present in serum from HAA-positive patients with immunodepressive states where they constituted 60-80% of the total number of particles found. Large numbers of Dane particles were found in 4 leukemia patients being treated with cytostatic agents, although the patients themselves had extremely mild hepatitis of short duration or no clinical symptoms of hepatitis. Although 6 patients who had undergone renal dialysis or who had kidney transplants had no symptoms of liver disease, members in 4 of the 6 families developed hepatitis. These facts tend to refute the hypothesis that Dane particles are associated with severe liver damage. HAA-associated particles were either grouped in aggregates or were present in disperse form. Since these aggregates were produced *in vitro* by addition of antibodies to HAA and since aggregates were never found in patients with immunodepressive states, these aggregates are probably not just artefacts, but may be immune complexes. HAA may also play a role in the pathogenesis of extrahepatic disease, such as immunodepressive states (periarteritis nodosa, glomerulonephritis).

7765 POST-KONYNE HEPATITIS: THE INEFFECTIVENESS OF SCREENING FOR THE HEPATITIS B ANTIGEN (HBAg). *(E.)* Sandler, S. G.; Rath, C. E.; Wickerhauser, M.; Dodd, R. Y.; Greenwalt, T. J. (Georgetown Univ. Hosp., Washington, D.C.). *Transfusion* 13(4):221-224, 1973.

Konyne (human factor IX complex) was given to 16 patients for bleeding episodes or for hemostasis during surgical procedures. These patients were subsequently evaluated for signs of post-transfusion hepatitis. Diagnoses in this series of patients included Laennec's cirrhosis (10), chronic active hepatitis (1), warfarin overdose (4), and hemophilia B (1). Primary disease caused death in 4 cases. Of the remaining 12 patients at risk, 6 developed post-transfusion hepatitis. Sera from 4 of the 6 with hepatitis were positive for the hepatitis B antigen (HBAg). Aliquots of Konyne from a specific lot implicated in 3 cases of HBAg-positive hepatitis were negative for HBAg by immunodiffusion, immunoelectroosmophoresis, and radioimmunoassay. The high incidence of hepatitis associated with Konyne considerably limits use of this specialized coagulation factor concentrate. HBAg screening by available technics does not necessarily detect Konyne preparations capable of transmitting HBAg-positive hepatitis.

7766 THE GENETIC RELATIONSHIPS OF AUSTRALIA ANTIGEN. *(E.)* London, W. T. (Inst. Cancer Res., Fox Chase, Philadelphia, Pa.). *Vox Sang.* [*Suppl.*] 24:1-7, 1973.

Australia antigen [Au(1)] has many characteristics of an infectious agent and many characteristics of an inherited serum protein polymorphism. In multiply transfused patients with thalassemia an association exists between antibodies to genetic markers on immunoglobulins, a known serum protein polymorphism, and antibodies to Australia antigen. Evidence is also available that Au itself is polymorphic; is composed of 5 or more polypeptides which are immunologically similar to normal human serum proteins (IgG, albumin, transferrin, β-lipoprotein, and the β-1a/1c-fraction of complement). Antigenic subtypes of Au have been demonstrated which appear to be inherited traits of the infectious agent. It is suggested that the manner in which an individual responds to ection with Au is determined by an interaction he host with the infectious agent which in is largely determined by the genetic make-up he host and the genetic composition of the t.

7 FACTORS INFLUENCING NEONATAL INFECTION BY HEPATITIS B VIRUS. *(E.)* Schweitzer, I. Mosley, J. W.; Ashcaval, M.; Edwards, V. M.; by, L. B. (Univ. Southern California, Sch. , Los Angeles). *Gastroenterology* 65(2):277- 1973.

titis B infection occurred and persisted in 13 7 infants whose mothers had acute hepatitis ng pregnancy or in the first 2 months postpar- This occurred in only 1 of 21 infants whose ers were asymptomatic carriers of hepatitis B gen. If the maternal icteric illness developed he first 2 trimesters, the rate of chronic neo- l infection (1 of 10) was not significantly dif- nt from that for carriers. The greater fre- cy of subtype ay as a cause of persistent infec- in infants was attributed to relative distri- on of ay and ad strains among acutely ill mothers carriers. Hepatitis B antigen of both subtypes sed the placenta equally. When the mother had genemia at delivery, counterelectrophoresis ed hepatitis B antigen was present in only 1 2 cord bloods. Radioimmunoassay gave positive lts in an additional 10. The presence of hepa- s B antigen in cord blood had no necessary rela- to subsequent antigenemia in the infant. It ars that the developmental period when exposure rs, rather than the clinical status of the er or the subtype, determines whether the in- will be chronically infected.

INTRAHEPATIC LOCALISATION OF AUSTRALIA ANTIGEN BY FLUORESCENT ANTIBODY TECHNIQUE. Muller, R.; Maess, J. (Hanover Med. Sch., any). *Vox Sang.* [*Suppl.*] 24:33-35, 1973.

nodiffusion and complement fixation techniques used to determine the intrahepatic presence of ralia antigen in the sera of patients with acute chronic hepatitis. In 9 patients with proven ralia antigenemia, intrahepatic localization of ralia antigen was demonstrated. Such localiza- was not found in any of 11 Australia antigen- tive controls. Australia antigen was found in the hepatocytes in 1 patient with posthepatic cirrhosis, in whom tests for Australia antigen consistently negative. In 6 specimens intra- ic fluorescence was revealed; in 4 liver biopsies e fluorescent granules within or on the surface e nuclei of the hepatocytes predominated. These ts support the theory that various patterns of hepatic localization of Australia antigen sig- different stages of intracellular accumulation e antigen and are not indicative of technical rences or differences in the specificity of ody to Australia antigen.

7769 HEMODIALYSIS-ASSOCIATED HEPATITIS. *(E.)* Garibaldi, R. A.; Forrest, J. N.; Bryan, J. A.; Hanson, B. F.; Dismukes, W. E. (Univ. Utah Med. Ctr., Salt Lake City). *JAMA* 225(4):384-389, 1973.

Of 65 renal hemodialysis units surveyed prospectively in a 4 yr period, 53 reported 355 cases of viral hepatitis - 260 in hemodialysis patients and 95 in hemodialysis unit staff members. The incidence of infection in the final yr of the study for center-based patients and staff was 4.4 cases/100 persons at risk and 3.4 cases/100 persons at risk, resp. The attack rate for patients having dialysis at home was only 1.2 cases/100 patients. Almost 70% of the 136 hemodialysis patients (78 males and 58 females, aged 25-50 yr) were anicteric; many would not have been detected if periodic serologic screening for hepatitis B antigen or liver-function tests had not been routine. Jaundice occurred in 85% of 65 staff members with hepatitis, and 74% required hospitalization. Routine liver studies were not performed on the staff. Although accidental needle punctures prior to hepatitis were reported by many staff, other types of exposures were common, and nonparenteral transmission probably occurred.

7770 HEPATITIS B VIRUS AND PERIARTERITIS NODOSA. *(Fr.)* Trepo, C. (Red Cross Hosp., Lyon, France). *Nouv. Presse Med.* 1(28):1879-1881, 1972.

Australia antigen (Au/SH) was detected in 24 patients with histologically verified periarteritis nodosa. In 17 cases the onset of the disease was characterized by symptoms of hepatitis (fever, arthralgia, myalgia, and increase in serum transaminase activities). The viral nature of the initial stage was confirmed by the presence of Au/SH, the results of punch liver biopsies, and a history of probable contamination by hepatitis virus in 15 cases. High titers of Au/SH were found early in the course of the disease, and the antigen persisted until death in all but 3 cases although signs of hepatitis regressed and transaminase values normalized. The titer of Au/SH decreased significantly during exacerbations in 2 cases. In 1 case the disappearance of Au/SH was associated with spontaneous recovery. This group was rather unusual since manifestations of hepatitis were common and pulmonary symptoms were rare. Tests for lupus erythematosis cells, antinuclear antibodies, and rheumatoid factor were negative in all cases. These findings demonstrate that the presence of Au/SH is not caused by superinfection with hepatitis B virus, as occurs in mongolism, but that hepatitis virus is involved in the induction and further course of periarteritis nodosa. However, since Au/SH is not detected in all patients with periarteritis nodosa, other causative factors must be implicated.

7771 PREVIOUSLY UNDESCRIBED PARTICLES IN Au-ASSOCIATED HEPATITIS. *(E.)* Johannessen, J. V.; Hamre, E. R. (Norwegian Radium Hosp., Oslo) *Lancet* (7823):258, 1973.

In the acute stage of a case of Australian antigen (Au)-associated hepatitis, previously undescribed virus-like particles were found in liver-cell nuclei. The particles stained with uranyl acetate. Despite some virus-like properties, they are not interpreted as virus particles but as aggregations of chromatin altered by the viral infection. It is believed that they represent a nonspecific result of liver cell damage. Particles similar to those usually referred to as Au particles have been described in tissues other than liver and in diseases other than viral hepatitis. It is possible that there is an immunological basis for the liver damage unassociated with viral replication in the liver itself.

7772 SIMILARITY OF HEPATITIS FOLLOWING TRANSFUSION OF AUSTRALIA-ANTIGEN POSITIVE AND NEGATIVE BLOOD. *(E.)* Sutnick, A. I.; Goeser, E.; Senior, J. R.; Millman, I. (Inst. Cancer Res., Philadelphia, Pa.). *Lancet* 2(7827):461-464, 1973.

Of 24 patients with post-transfusion hepatitis, 12 had received at least 1 unit of Australia-antigen (Au)-containing blood, and 12 had received only blood in which the antigen was not detected. By immunodiffusion, 7 of the 12 Au recipients and none of the recipients of negative blood developed detectable serum-Au, and 1 developed antibody. By radioimmunoassay these figures became 8 and 9, resp. The 2 groups had similar symptoms and signs; 3 of the Au recipients and 4 of the Au-negative recipients became jaundiced. Median incubation period in Au cases was 51 days (range 17-132), and in Au-negative cases, 62.5 days (range 42-94). This was not a significant difference, nor was there any difference in the time to reach maximum SGPT or the duration of SGPT elevation. The maximum SGPT level was similar in the 2 groups, as was the maximum serum bilirubin and prothrombin time, and no histological distinction could be made. The median peak serum alkaline phosphatase in the Au recipients was 41 I.U., and in the Au-negative blood recipients, 113.5 I.U. With this sole exception, these findings indicate that there are no distinguishing features between the hepatitis occurring in patients receiving Au-positive blood and that occurring in recipients of Au-negative blood with regard to incubation period, symptoms, physical findings, clinical course, laboratory findings, and severity of disease.

7773 RELATION BETWEEN VIRAL HEPATITIS AND BONE MARROW APLASIA. *(Ger.)* Stieglitz, R. (1st Med. Clin., Humboldt Univ., Berlin, Germany). *Z. Aerztl. Fortbild.* 65(21):1131-1135, 1972.

A survey of the literature reveals that during the past 3 yr bone marrow aplasia has been reported as a sequela of viral hepatitis in 50 patients. These included 32 males and 14 females; sex was not reported in 4 cases. Although the patients ranged in age from 2 to 74 yr, this sequela appears to occur primarily in teen-aged boys. The interval between the onset of hepatitis and that of bone marrow aplasia ranged from less than 1 week to 7 months, with several weeks being the most commonly reported interval. Of these patients, 34 died, 3 recovered, 2 are still recovering, and 1 still has bone marrow hypoplasia; the outcome could not be ascertained in the remaining cases. Chloramphenicol was implicated in 4 cases. Liver findings included dystrophy (2), cirrhosis (3), necrosis (3), and chronic hepatitis (1). One patient developed a recurrence of bone marrow aplasia when hepatitis recurred. Antibodies against platelets were reported in 5 cases, against WBC in 4 cases, and against RBC in 1 case. Immunological and allergic mechanisms may be involved in the pathogenesis of this type of bone marrow aplasia, or it may be due to direct damage produced in bone marrow by the virus.

7774 LYMPHOCYTE FUNCTION IN NORMAL PEOPLE WITH PERSISTENT AUSTRALIA ANTIGEN. *(E.)* Sutnick, A. I.; Bugbee, S. J.; London, W. T.; Foeb, L. A.; Peyretti, F.; Litwin, S.; Blumberg, B. S. (Fox Chase Ctr. Cancer, Philadelphia, Pa.). *J. Lab. Clin. Med.* 82(1):79-85, 1973.

To determine whether impaired lymphocyte function is related to susceptibility to persistance of Australian antigen [Au(1)], 2 populations living in the same environment, the city of Turin, Italy, were tested. The Sardinian group has a known high frequency of persistent Au(1) (up to 10%) and was considered a susceptible population. The Turinese group has a low frequency (0.5%) and was considered the control population. The study was performed in a series of 14 age- and sex-matched quartets, 2 Sardinians and 2 Turinese, each with and without Au(1). Lymphocyte function was evaluated by culturing the cells with phytohemagglutinin, and quantitating DNA synthesis by measuring the incorporation of ^{3}H-thymidine and assaying DNA polymerase activity. No differences were found between the Sardinians and Turinese, implying that the lymphocyte deficit is not the basis for susceptibility to persistence of Au(1). The reason for the difference in the frequency of the Au(1) carrier state between the 2 populations is unknown. Lymphocyte function was also similar in the subjects with and without Au(1), indicating that Au(1) *per se* in a normal host does not impair lymphocyte response. Since such impairment is found in other diseases associated with persistent Au(1) (Down's syndrome, leukemia, Hodgkin's disease, lepromatous leprosy, and chronic renal disease), the lymphocyte abnormality likely results from these underlying disorders.

7775 JEJUNAL BRUSH BORDER DISACCHARIDASE AND ALKALINE PHOSPHATASE ACTIVITY IN ACUTE VIRAL HEPATITIS. *(E.)* Gudmand-Hoyer, E.; Soeberg, B. (Blegdams Hosp., Copenhagen, Denmark). *Scand. J. Gastroenterol.* 31(3):377-380, 1973.

A group of 11 patients (2 females and 9 males, aged 14 to 37 yr) were diagnosed as suffering from inoculation hepatitis (4) or from epidemic hepatitis (7). Stereomicroscopy of jejunal biopsy specimens showed

at in only 1 patient did a pronounced villous
rophy occur sporadically. Light-microscopy re-
aled an additional 3 patients had an increased
llular infiltration. A lower enzyme activity was
und in hepatitis patients as compared with controls.
e difference was significant in the case of sucrase,
ltase, and alkaline phosphatase. Although there
s a general correspondence between reduced enzyme
tivity and abnormal microscopic findings, enzyme
tivity was not related to the duration of the jaun-
ce, the presence of Australian antigen, or the
pe of viral hepatitis.

76 NATIONAL COOPERATIVE STUDY OF HEPATITIS B
ANTIBODY TREATMENT OF ANTIGEN-POSITIVE FUL-
NANT HEPATITIS: FIRST RANDOMIZED CASE IN ILLINOIS.
.) Clowdus, B. F.; Steigmann, F.; Vittal, S.;
urourekas, D. (Hepatitis Coordinating Ctr., Hektoen
st. Med. Res., Chicago, Ill.). *Ill. Med. J.* 143
):515-518, 1973.

22 yr old white female nurse was pricked by a
edle used on a dialysis patient positive for Austra-
a antigen. No gamma globulin was administered.
ter a time, a sore throat and malaise developed.
usea followed and jaundice was noted 4 days later,
which time total serum bilirubin was 11.5; SGOT,
30; and SGPT, 7250. Early in the morning of the
cond hospital day she was in Stage IV hepatic
ma: blood urea nitrogen (BUN) was 0; prothrombin
me, 16% of normal; HBAg, positive; HBAb, negative.
fusion of human serum protein presumably containing
patitis B immune globulin was started, and con-
ued for 70 min. There were no immediate or later
verse effects. At 10 hr post-infusion, prothrom-
 time was 17% of normal. At 27 hr, there was
ght response to verbal stimuli: BUN was 0; pro-
rombin time, 21% of normal; HGAB positive. By 87
 the prothrombin time was 39% of normal; BUN, 3;
al serum bilirubin, 11 mg/100 ml; and SGOT, 135.
rotein-free carbohydrate diet was started. The
ient was discharged 543 hr post-infusion. It is
gested that physicians desirous of obtaining this
eatment for a patient should contact the Hepatitis
rdinating Center of the Hektoen Institute.

7 TRANSMISSION OF TYPE B VIRAL HEPATITIS TO
CHIMPANZEES. *(E.)* Barker, L. F.; Chisari,
V.; McGrath, P. P.; Dalgard, D. W.; Kirschstein,
L.; Almeida, J. D.; Edgington, T. S.; Sharp, D.
 Peterson, M. R. (Div. Vir., Bur. Biologics,
, Rockville, Md.). *J. Infect. Dis.* 127(6):648-
, 1973.

6 chimpanzees inoculated with materials positive
 hepatitis B antigen (HB Ag), 5 developed evi-
ce of hepatitis B virus infection. In 2 of the
here was serologic, biochemical, and histologic
dence of type B viral hepatitis accompanying in-
tion. HB Ag in the cytoplasm of hepatocytes and
atitis B virus-associated core antigen (HBC Ag)
 virus-like particles in some hepatocyte nuclei
e found by immunofluorescence and electron micros-
y. Of the remaining 3 animals, 2 developed transient circulating HB Ag followed by antibody to HB Ag (HB Ab), and the 3rd developed HB Ab in serum approximately 3 months after inoculation without any biochemical or histologic evidence of disease. Of the 5 infected animals, 3 represented a 2nd passage of hepatitis B virus from a chimpanzee infected with plasma known to transmit type B viral hepatitis to man. Evidence of infection of 1 of these 3 animals included demonstration of the presence of the hepatitis B virus in a preparation of HB Ag that had been partially purified by isopycnic banding in a continuous sucrose gradient. Fluorescent staining of liver tissue from a chimpanzee shown to be a chronic carrier of HB Ag revealed HB Ag in the cytoplasm of most cells and HBC Ag rarely in cell nuclei; no virus-like particles in hepatocyte nuclei or liver histopathology were observed. This study suggests that the chimpanzee would be a good model for studying protective immunity as well as pathogenesis and the carrier state of type B viral hepatitis.

7778 HEPATITIS IN DIALYSIS UNITS IN THE UNITED KINGDOM. *(E.)* Polakoff, S.; Cossart, Y. E.; Tillett, H. E. (Public Hlth. Lab. Service, London, England). *Br. Med. J.* 3(5871):94-99, 1972.

A prospective study of hepatitis in 20 dialysis units showed that the number of units with outbreaks increased from 1 in 1968 to 3 in 1969 and the overall attack rate rose from 1.7 to 5.3% in patients and from 0.5 to 1.3% in staff during that time. A July 1969 pilot study of patients' sera showed that all of the outbreaks were associated with Australia (Au) antigen. Au antigen was not detected in the unaffected units or in 1 unit in which there were several patients with abnormal liver function. The results of this study also confirmed the tendency of patients with chronic renal failure to become long-term carriers with little biochemical evidence of liver disease. Systematic prospective testing for Au antigen was begun in January 1970. Au antigen was detected in single patients in 5 more of the 20 units. The transfer of the affected patients to isolation for dialysis seemed to prevent the spread of infection in the units. The incidence of hepatitis in 1970 was 5.6% in patients and 0.4% in staff.

7779 ACUTE VIRAL HEPATITIS, AUSTRALIA ANTIGEN, AND CHROMOSOMES. *(Ger.)* Vormittag, W.; Paumgartner, G. (2nd Med. Clin., Univ. Vienna, Austria). *Klin. Wochenschr.* 51(9):445-449, 1973.

Karyotypes were obtained on lymphocyte cultures from the peripheral blood of 11 patients (9 men and 2 women, aged 21-69 yr) during various stages of viral hepatitis and after normalization of laboratory findings. Relations between chromosome abnormalities, Australia antigen (HAA), and laboratory findings were investigated. During the acute stage of hepatitis the number of metaphases with chromosome aberrations was 21.5 ± 6.74% in HAA-positive patients and 7.2 ± 3.03% in HAA-negative patients; this difference is highly significant. The aberration rate was only 3.2 ± 2.14%

in 10 controls with polyarthritis and no evidence of liver disease; this rate differed significantly from rates established for both HAA-positive and HAA-negative patients. In 9 patients the aberration rate decreased rapidly after 1-3 weeks as HAA titers decreased rapidly. The aberration rate remained high in 1 patient with persistently high titers of HAA; in another patient who was still HAA-positive at 7 weeks the aberration rate decreased rapidly during the first 3 weeks but subsequently increased again to its initial value. This finding could be explained by a combination of continuing cell damage and persistence of damaged cells in the peripheral blood or by a continuous and persistent release of damaged cells from lymphatic tissue into the blood. High aberration rates were found on several occasions in only 1 HAA-negative patient. Chromosome aberrations found in patients with viral hepatitis consisted primarily of gaps and chromatid breaks, but a few isogaps and chromosome breaks were also detected. Aberrations were most common among A and B group chromosomes. No clear correlations were established between chromosome aberrations rates and SGOT or bilirubin values. Age, medication, a history of recent exposure to radiation, and severity of the hepatitis had no demonstrable effect on the aberration rate. It is suggested that the persistence of high chromosome aberration rates in HAA-positive patients could be evidence for the carcinogenic effect of hepatitis virus.

7780 SEROLOGICAL AND EPIDEMIOLOGICAL STUDIES OF HEPATITIS B IN HAEMODIALYSIS UNITS. *(E.)* Pattison, C. P.; Maynard, J. E.; Berquist, K. R.; Webster, H. M. (Ctr. Dis. Control., Phoenix, Ariz.). *Lancet* (7822):172-174, 1973.

Further to clarify the epidemiology of dialysis-unit hepatitis, serological sampling for hepatitis-B antigen (HBAg) and antibody (HBAb) by radioimmunoassay was carried out in 4 hemodialysis units with no epidemic history of hepatitis. Of 99 patients, 6% were seropositive for HBAg, 29% for HBAb, and 1 patient had both. Of 55 staff members, 2% were seropositive for HBAg, 35% for HbAb, and 1 staff member had both. Of 65 persons having family contacts with the patients, 3% were seropositive for HGAg and 11% for HBAb. Of 21 persons having family contacts with the staff members, 10% were seropositive for HBAb. Thus, family contacts of patients and staff showed no significantly greater infection prevalence (13%) than did any of the 3 control populations, but spouses of seropositive index cases (patients or staff) did seem to be at higher risk for secondary infection with type-B viral hepatitis. Patients undergoing dialysis 3 or more times/week had a much higher infection prevalence (42%) than those dialyzed less than 3 days/week (21%). The frequency of seropositivity was 44% in those who dialyzed for 6 hr or less each time and 21% in those dialyses lasting more than 6 hr. Among the staff, 6.7% of the housekeeping personnel were seropositive compared with only 20% of the doctors and clerical staff. This argues against the theory of airborne transmission as a major mechanism of spread. Prevalence of seropositivity was higher (57%) among dialysis-unit personnel who did not wear gloves when dialyzing than among those who took the precaution (22%). Although transfusion of blood products did correlate with infection prevalence, these results suggest the dialyzer may be a potent factor in disease transmission.

7781 PRIMATES AS A MODEL FOR HUMAN VIRAL HEPATITIS: TRANSMISSION OF INFECTION BY HUMAN HEPATITIS B VIRUS. *(E.)* Desmyter, J.; Liu, W. T.; De Somer, P.; Mortelmans, J. (Rega Inst. Med. Res., Louvain, Belgium). *Vox Sang.* [*Suppl.*] 24:17-26, 1973.

The incidence and transmission of Australia antigen and antibody were investigated in 48 nonanthropoid primates belonging to 14 species, 2 orangutans, 2 gorillas, 3 dwarf chimpanzees, and 50 chimpanzees. With complement fixation, Australia antigen was detected in 1, and antibody in 6, of 50 chimpanzees. Negative results were found in 7 other apes, and 48 monkeys. All postive chimpanzees clustered in 1 colony comprising 15 animals, and antibody titers decreased simultaneously over a period of several months. This finding indicates an infectious pattern of Australia antigenemia and antibodies in chimpanzees. Antigen and antibodies were undistinguishable from those of man. Australia antigen-positive serum from a contagious human carrier was injected in 5 chimpanzees. In 1 chimpanzee, with antibody before, but not at the time of exposure, circulating antibodies developed after 13 weeks, followed by antigenemia, antigen-antibody complexes, increased transaminase levels and slightly aboormal liver histology. In 1 antibody reaction occurred chimpanzee, without spontaneous antibody, after

abnormal liver histology. In 1 chimpanzee, without spontaneous antibody, an antibody reaction occurred after 8 weeks, suggesting active infection. No proof of infection was obtained in 3 other animals. These results suggest that chimpanzees are susceptible to infection by human hepatitis B virus, that liver damage is less pronounced than in humans, and that previous spontaneous experience with Australia antige modifies, but does not entirely suppress, the infection. The chimpanzee is the model of choice for study of various aspects of viral hepatitis type B.

7782 RECOGNITION OF HEPATITIS B ANTIGEN DETERMINANTS BY A DOUBLE LABEL RADIOIMMUNOASSAY: A SENSITIVE MEANS OF SUBTYPING HEPATITIS B ANTIGEN. *(E.)* Aach, R. D.; Hacker, E. J.; Parker C. W. (Washington Univ. Sch. Med., St. Louis, Mo.). *J. Immunol.* 111(2):381-388, 1973.

A sensitive radioimmunoassay was developed for subtyping hepatitis B antigen (HB Ag) in human serum. The method uses antisera (HB Ab), prepared in immunized guinea pigs, which contain predominantly anti-d or anti-y antibodies, and radioiodinated HB Ag of either D or Y subtype. Sera with HB Ag of subtype D (D) were strongly positive by radioimmunoassay, employing anti-d HB Ab and ^{125}I-HB Ag (D); specimens with HB Ag of Y subtype were negative or only weakly positive. Converse results were observed when antigenemic sera were evaluated by radioimmunoassay with anti-y HB Ab and ^{125}I Y. By combining guinea pig HB Ab possessing high-titered anti-d and anti-y with ^{131}I D and ^{125}I Y, it was possible to screen for and subtype HB Ag simultaneously. Antigenemic sera from 105 samples were evaluated; 93 or 88% could be readily subtyped by the combined radioimmunoassay, including 31 of 43 samples with HB Ag in amounts too low to be detected by agar gel difusion or counter immunoelectrophoresis. Subtype D-HB Ag occurred primarily in serum of blood donors and patients with posttransfusion hepatitis. Subtype Y antigen predominated in hepatic individuals associated with illicit drug use. Samples showing only "a" specificity by agar gel diffusion also possessed "d" or "y" determinants by radioimmunoassay. The relative antigenic reactivity of "a" and "d", or "a" and "y" determinants appeared to vary in different specimens. This could not be explained by the HB Ag subtype or the number of particles in the specimens evaluated.

7783 VIRAL HEPATITIS: ANOTHER ATTEMPT AT MASS PREVENTION WITH GAMMA GLOBULIN. *(Fr.)* Laverdant, C.; Antoine, H.; Nicolle, R.; Molinie, C.; Cristau, P.; Gautier, D. (Army Training Hosp., St. Mande, France). *Nouv. Presse Med.* 2(10):639-640, 1973.

7784 NEW ASPECTS OF INFECTIOUS HEPATITIS WITH SPECIAL CONSIDERATION OF AUSTRALIA ANTIGEN. *(Ger.)* Schneeweiss, B.; Tacke, A.; Geserick, G.; Alvermann, B.; Steinruck, H. (Pediatr. Clin., Humboldt Univ., Berlin, Germany). *Paediatr. Grenzgeb.* 11(3):189-194, 1972.

7785 SERUM CHOLINESTERASE AS A TEST OF LIVER CELL FAILURE. *(Fr.)* Tamarelle, C.; Quinton, A.; Bancons, J.; Dubarry, J. J. (Saint-Andre Hosp., Bordeaux, France). *Sem. Hop. Paris* 49(12):859-864, 1973.

7786 AN IN VITRO STUDY OF THE ACTIVITY AGAINST AUSTRALIA ANTIGEN OF VARIOUS PREPARATIONS OF IgG. *(E.)* Gortz, J. P. (Res. Lab. Natl. Inst. Blood, Brussels, Belgium). *Vox Sang.* [*Suppl.*] 24:137-140, 1973.

7787 SPECTRUM OF FREE AMINO ACIDS IN THE SERUM OF PATIENTS WITH INFECTIOUS HEPATITIS. *(Rus.)* Triapyshko, A. D. (Saratov Med. Inst., USSR). *Vrach. Delo* (7):137-140, 1973.

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7789 AUSTRALIA ANTIGEN AND ITS RELATION TO VIRAL HEPATITIS. LITERATURE REVIEW. *(Rus.)* Golosova, T. V.; Margolina, A. N. (Central Inst. Hematol. Blood Transfusion, Moscow, USSR). *Lab. Delo* (6):323-327, 1973.

7790 AUSTRALIA ANTIGEN: CLINICAL STUDY OF METHODS FOR ITS DETECTION AND CONSEQUENCES IN PATHOPHYSIOLOGICAL INTERPRETATION OF VIRAL HEPATITIS. *(Fr.)* Delmas-Marsalet, Y.; Paris, J. C.; Lobry, C.; Filoche, B.; Bleuet, M.; Hazard, C. (Univ. Hosp. Ctr., Lille, France). *Lille Med.* 17(7):960-963, 1972.

7791 AUSTRALIA ANTIGEN IN VARIOUS ASPECTS OF HEPATITIS: PROGNOSTIC VALUE. *(Fr.)* Tete, R.; Barthe, J.; Trepo, C.; Vachon, A. (Hotel Dieu, Lyon, France). *Lyon Med.* 229(1):43-52, 1973.

7792 EXTRACORPOREAL PERFUSION WITH ANIMAL LIVERS IN THE TREATMENT OF PATIENTS IN COMAS COMPLICATING VIRAL HEPATITIS. *(It.)* Kassur, B.; Oleinik, Z. (Acad. Med., Warsaw, Poland). *Minerva Med.* 64(9):429-435, 1973.

7793 DETERMINATION OF AUSTRALIA ANTIGEN SUBTYPES. *(Fr.)* Courouce-Pauty, A. M.; Soulier, J. P. (Natl. Ctr. Blood Transfusion, Paris, France). *Nouv. Presse Med.* 2(10):629-633, 1973.

7794 VIRAL HEPATITIS AND BONE MARROW APLASIA: ONE CASE REPORT. *(Fr.)* Blanchon, P.; Paillas, J.; Holler, A.; Allard, C.; Larrieu, C. (Bicetre Hosp., France). *Ann. Med. Interne (Paris)* 124(6/7):529-534, 1973.

7795 CHANGES IN PLASMA RENIN ACTIVITY DURING VIRAL HEPATITIS. *(It.)* Antonello, A.; Favaro, S.; Baggio, B.; Cadrobbi, P.; Todesco, S.; Borsatti, A.; Naccarato, R. (Inst. Special Med. Pathol. Clin. Methodology, Univ. Padua, Italy). *Boll. Soc. Ital. Biol. Sper.* 48(12):307-309, 1972.

7796 VISUALIZATION OF THE "NETWORK" PHENOMENON BETWEEN AUSTRALIA ANTIGEN AND ANTI-Au ANTIBODIES (IN VITRO AND IN VIVO). *(Fr.)* Couleru, O.; Moulias, R. (no affil.). *C. R. Acad. Sci. (Paris)* 275(13):1457-1458, 1972.

7797 TEMPORARY SUPPRESSION OF THE QUATERNARY STRUCTURE OF PLASMA ALPHA-LIPOPROTEINS (HDL) AT THE ONSET OF COMMON VIRAL HEPATITIS. *(Fr.)*

Hartmann, L.; Abelanet, R.; Ollier, M. P.; Fiessinger, J. N. (Med. Sch., Paris, France). *C. R. Acad. Sci. (Paris)* 276(8):2597-2600, 1973.

7798 SEVERE VIRAL HEPATITIS. *(Fr.)* Sicot, C. (Beaujon Hosp., Clichy, France). *Concours Med.* 95(18):3251-3261, 1973.

7799 DIFFERENCES IN THE PREVALENCE OF HEPATITIS B ANTIGEN AND ANTIBODY AMONG PANAMANIAN INDIAN POPULATIONS. *(E.)* Reeves, W. C.; Peters, C. J.; Lander, J. J.; Purcell, R. H.; Johnson, K. M. (Natl. Inst. Allergy Infec. Dis., NIH, Balboa Heights, Canal Zone). *J. Infect. Dis.* 128(3):265-270, 1973.

7800 RECENT ADVANCES IN OUR UNDERSTANDING OF HEPATITIS B INFECTIONS. *(E.)* Prince, A. M.; Szmuness, W.; Brotman, B.; Ikram, H. (New York Blood Ctr., N.Y.). *Vox Sang.* [*Suppl.*] 24:8-16, 1973.

7801 ADVANCES IN VIRAL HEPATITIS. *(E.)* Zuckerman, A. J. (London Sch. Hyg. Trop. Med., England). *Clin. Med.* 80(7):11-18, 1973.

7802 AUSTRALIA ANTIGEN IN CORD BLOOD. *(E.)* Krech, U.; Sonnabend, W.; Kristler, G.; Mader, A. (Inst. Bacteriol., Zurich, Switzerland). *Vox Sang.* [*Suppl.*] 24:55-60, 1973.

7803 INCIDENCE OF HEPATITIS AFTER EXCHANGE TRANSFUSIONS IN NEWBORNS. *(Ger.)* Schaub, G.; Stroder, J. (Child. Clin., Univ. Wurzburg, Germany). *Klin. Wochenschr.* 59(16):788-789, 1972.

7804 FREQUENCY OF AUSTRALIA ANTIGEN DETECTED BY RADIOIMMUNOASSAY IN HEPATITIS IN CHILDREN. *(E.)* Chiba, S.; Fujiwara, T.; Shiono, H.; Nakao, T. (Sapporo Med. Coll., Japan). *Tohoku J. Exp. Med.* 109(3):307-308, 1973.

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7806 SUBTYPES OF HEPATITIS B ANTIGEN AMONG ISRAELI BLOOD DONORS. *(E.)* Bar Shany, S.; Edwards, V. M.; Mosley, J. W.; Bancroft, W. H. (Central Blood Bank, Tel Aviv, Israel). *Vox Sang.* 25(2):105-112, 1973.

7807 SYMPTOMATIC ACUTE AUTOIMMUNE HAEMOLYTIC ANAEMIA WITH INCOMPLETE THERMO-AUTO-ANTIBODIES IN ACUTE HEPATITIS. *(Ger.)* Wagner, K.; Wagner, W. (no affil.). *Wien. Klin. Wochenschr.* 85(33-34):564-566, 1973.

7808 PROGRESS REPORT ON VIRAL HEPATITIS. *(E.)* Zuckerman, A. J. (Virol. Dept., Univ. London, England). *Trop. Doctor* 3(4):150-154, 1973.

7809 THE EPIDEMIOLOGY OF HEPATITIS B INFECTIONS IN AFRICA: RESULTS OF A PILOT SURVEY IN THE REPUBLIC OF SENEGAL. *(E.)* Szmuness, W.; Prince, A. M.; Diebolt, G.; Leblanc, L.; Baylet, R.; Masseyeff, R.; Linhard, J. (New York Blood Ctr., N.Y.). *Am. J. Epidemiol.* 98(2):104-110, 1973.

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7811 AUSTRALIA ANTIGEN AU(1) IN SCHOOL CHILDREN IN IBADAN, NIGERIA. *(E.)* Francis, T. I.; Smith, J. A. (Univ. Coll. Hosp., Ibadan, Nigeria). *J. Trop. Med. Hyg.* 76(1):19-22, 1973.

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7814 PERMANENT LIVER DAMAGE AFTER INFECTIOUS MONONUCLEOSIS. *(Ger.)* Stejskal, J.; Osleskova, M.; Snopkova, J. (Clin. Pediatric Infections, J. E. Purkyne Univ., Brno, Czechoslovakia). *Monatsschr. Kinderheilkd.* 121(6):231-234, 1973.

7815 DUALITY OF HEPATITIS B ANTIGEN AND ITS ANTIBODY. I. IMMUNOFLUORESCENCE STUDIES. *(E.)* Brzosko, W. J.; Madalinski, K.; Krawczynski, K.; Nowoslawski, A. (State Inst. Hyg., Warsaw, Poland). *J. Infect. Dis.* 127(4):424-428, 1973.

7816 RELATION BETWEEN BLOOD GROUPS AND HEPATITIS ASSOCIATED ANTIGEN CARRIER STATE. *(E.)* Hadziyannis, S.; Papevangelou, G.; Vissoulis, C. (2nd Dept. Med., Univ. Athens, Greece). *Vox. Sang.* 24(1):89-93, 1973.

317 LIVER NECROSIS, ADENOVIRUS TYPE 2 AND THYMIC DYSPLASIA. *(E.)* Aterman, K.; bil, J.; Easterbrook, K. B.; Haldane, E. V.; osby, J. (Dept. Pathol., Univ. Dalhousie, lifax, Canada). *Virchows Arch.* [*Pathol. Anat.*] 0:155-171, 1973.

318 AUSTRALIA ANTIGEN AND POSTTRANSFUSION HEPATITIS. A STUDY OF DANISH BLOOD DONORS D RECIPIENTS. *(E.)* Reinicke, V.; Banke, O.; bkjaer, E. (Bispebjerg Hosp., Copenhagen, nmark. *Vox Sang.* [*Suppl.*] 24:65-71, 1973.

319 TISSUE AND ORGAN CULTURE STUDIES OF HEPATITIS TYPE B. *(E.)* Zuckerman, A. J.; rl, P. M. (London Sch. Hyg. Trop. Med., England). *x Sang.* [*Suppl.*] 24:123-128, 1973.

320 AUSTRALIA ANTIGEN AND ANTIBODY IN LABORATORY AND OTHER HOSPITAL PERSONNEL. *(E.)* nst, V. A. J. M.; Bloo, J. H. (Univ. Hosp., jmegen, Netherlands). *Vox Sang.* [*Suppl.*] :61-64, 1973.

321 AUSTRALIA ANTIGEN: CURRENT CONCEPTS. *(E.)* Frohlich, J. (no affil.). *Hawaii Med. J.* (3):161-164, 1973.

322 THE FREQUENCY OF HEPATITIS ASSOCIATED ANTIGEN AND ANTIBODY IN PATIENTS WITH PARAPRO-INEMIA. *(E.)* Riesen, W.; Butler, R.; Skvaril, F.; seda, G.; Castel, V.; Barandun, S. (Inst. Clin. p. Cancer Res., Berne, Switzerland). *Vox Sang.* :477-480, 1973.

323 HEPATITIS B VIRUS ANTIGEN DETECTION BY REVERSE PASSIVE HEMAGGLUTINATION. *(E.)* rata, A. A.; Emerick, A. J.; Boley, W. F. (Abbott Lab., North Chicago, Ill.). *Proc. Soc. Exp. ol. Med.* 143(3):761-763, 1973.

324 INTRAHEPATIC FOCAL LESION IN ACUTE VIRAL HEPATITIS. *(E.)* Koenigsberg, M.; Freeman, . M. (Albert Einstein Coll. Med., Bronx, N.Y.). *Nucl. Med.* 14(8):612-614, 1973.

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7826 HEPATITIS EPIDEMIC IN A HYPERENDEMIC ZONE OF COSTA RICA. REPORT OF A SECOND OUTBREAK WITHIN FOUR YEARS. *(E.)* Villarejos, V. M.; Arguedas, J. A.; Gutierrez, A.; Eduarte, E.; Vargas, G.; Osborne, J. A. (Louisiana State Univ. Internatl. Ctr. Med. Res. Tr., San Jose, Costa Rica). *Am. J. Epidemiol.* 96(5):361-371, 1972.

7827 VIRAL HEPATITIS. RISK FOR THE PATIENT AND THE STAFF DURING EXTRA CORPOREAL CIRCULATION. *(Fr.)* Weiss, M.; Guiard, J.; Planche, C.; Guilleret, C. (Surg. Ctr. Marie-Lannelongue, Paris, France). *Nouv. Presse Med.* 2(21):1437-1441, 1973.

7828 DIALYSIS HEPATITIS. EFFECTS OF THE RENAL GRAFT. *(Fr.)* Dusart, D.; De Roy, G.; Thiry, L.; Clinet, G.; Toussaint, C. (Brugmann Hosp., Brussells, Belgium). *Acta Gastroenterol. Belg.* 35(9):357-370, 1972.

See also, 6734, 6764, 6768, 6770, 6772, 6790, 6793, 6800, 6801, 6802, 6821, 6842, 6864, 6874, 6877, 6883, 7928, 7945, 7972, 8205.

LIVER AND BILIARY TRACT

Chronic Hepatitis

829 THE PREVALANCE OF FATTY LIVER IN BIOPSIED MATERIAL. *(Ger.)* Kuhn, G.; Niedobitek, F. ed. Acad., Lubeck, Germany). *Z. Gastroenterol.* (3):181-188, 1972.

Fatty liver was detected in 653 of 2083 patients autopsied in 1967-1969. Of these 653 patients, 475 (72.7%) were men and 178 (27.3%) were women. The prevalence of fatty liver increased from 165 cases (26.7%) in 1967 to 274 cases (35.6%) in 1969. While only 42 (2.0%) of the patients with fatty liver had acute viral hepatitis, 266 patients (12.8%) had chronic hepatitis. Cholestasis and cholangitis were found in 82 of 653 patients with fatty liver (3.8%); siderosis, ranging from mild to pronounced, was present in 336 patients (51.5%); and mesenchymal changes were found in 292 (30.4%). Clinical histories of alcoholism were obtained in 255 cases (39.1%). Mallory bodies were present in the livers of most of these alcoholics, but they were not specific for alcoholic liver disease. Extensive mesenchymal changes were detected in 169 of the 255 alcoholics with fatty liver: these included 23 (9.0%) with associated cirrhosis and 146 (57.3%) with associated hepatitis. Histological evidence of latent or manifest diabetes was obtained in 114 cases. Since 28 of the 114 diabetics also had a history of alcoholism, only 86 cases (13.2%) of fatty liver can be attributed to diabetes alone. Siderosis was detected in about 2/3 of the 255 alcoholics. Mesenchymal changes were much less pronounced in diabetic than in alcoholic fatty liver.

7830 DOUBLE-BLIND STUDY OF LACTULOSE IN 18 PATIENTS WITH CHRONIC LIVER COMA AFTER PORTOCAVAL SHUNT SURGERY.

(Fr.) Germain, L.; Frexinos, J.; Louis, A.; Ribet, A. (Purpan Hosp., Toulouse, France). *Arch. Fr. Mal. App. Dig.* 62(4):293-302, 1973.

A group of 18 outpatients (13 men and 5 women, aged 18-67 yr) who had undergone shunt surgery 4 months to 7 yr before for chronic hepatic coma were randomly divided into 2 groups. The first group included 5 men and 2 women, aged 39-65 yr, with end-to-side portocaval anastomoses and 2 men, aged 20 and 50 yr, resp. with end-to-side splenorenal anastomoses. Each patient in this group received 60 ml/day of a 50% lactose solution for 15 days. A control group of 2 men and 2 women, aged 49-61 yr. with end-to-side portacaval anastomoses and 4 men and 1 woman, aged 18-63 yr, with end-to-side splenorenal anastomoses received a placebo containing sucrose. Statistical analysis of results showed no significant differences between the clinical symptoms or blood ammonia levels in lactose treated patients and controls. However, the results of psychometric tests were better and electroencephalograms showed significantly more improvement in the lactose-treated group. Transient diarrhea (3 cases) was the only side effect which occurred; hypokalemia was not observed. It is pointed out that the 2 groups of patients are not strictly comparable since they were not matched for the type of shunt operation performed or the severity of clinical symptoms.

7831 IMMUNOLOGICAL DIAGNOSIS OF PROGRESSIVE LIVER DISEASE.

(It.) Danieli, G.; Malini, P. L.; Dal Monte, P. R.; Montroni, M.; La Placa, R. (2nd Inst. Med. Pathol., Univ. Bologna, Italy). *Minerva Med.* 64(13):608-612, 1973.

Immunological tests were run on 64 patients with chronic liver disease. These consisted of 33 with alcoholic cirrhosis, 17 with postnecrotic cirrhosis, 11 with chronic active hepatitis, and 3 with primary biliary cirrhosis. Total immunoglobulin was increased in about 80% of the patients and was present in very high levels in postnecrotic cirrhosis. Neither total immunoglobulin, immunoglobulin fractions, fusion of β_2- and γ-globulins, antinuclear factor, antimitochondrial antibody, anti-smooth muscle antibody, rheumatoid factor, serum complement, nor complement fixation in the presence of liver or kidney homogenate was specific for any form of chronic liver disease. It is concluded that histological examination of biopsies is the best method for diagnosing chronic liver disease.

7832 HEPATITIS B ANTIGEN (HB Ag)-POSITIVE CHRONIC AGGRESSIVE HEPATITIS AND CIRRHOSIS IN AN 8-MONTH-OLD INFANT: A CASE REPORT.

(E.) McCarthy, J. W. (United States Army Med. Ctr., Fort Gordon, Ga.). *J. Pediatr.* 83(4):638-639, 1973.

A white female, aged 18 months, presented with severe jaundice. The infant's skin had been icteric at birth with scleral icterus noted at 3 months and dark urine from 5 months. Total and direct bilirubin SGOT, and alkaline phosphatase were elevated. The mother had received a blood transfusion 6 yr earlier, and both mother and child were positive for Australia antigen. Liver biopsy revealed distorted thickened hepatic cords with hepatocyte degeneration and chronic inflammation. Increased fibrous connective tissue was observed in the portal zones and connective tissue infiltrates of limiting plates with pseudolobular formation. A diagnosis of chronic aggressive hepatitis with cirrhosis was established. Prednisone therapy was given for 3 months, after which azathioprine was then added due to continued evidence of active disease. The mother's history of a transfusion plus the presence of Australia antigen in both mother and infant suggests perinatal transmission of Australia antigen and hepatitis from mother to child. This case shows that neonatal hepatitis with persistent Australia antigen can progress as chronic aggressive hepatitis to cirrhosis. It is suggested that a history of hepatitis in infancy plus a persistent Australia antigen calls for extensive evaluation of the patient to determine if chronic aggressive hepatitis is present.

7833 AUSTRALIA ANTIGEN AND CIRCULATING ANTIBODIES IN CHRONIC AGGRESSIVE HEPATITIS.

(E.) Findor, J.; Bruch Igartua, E.; Alonso, A.; Domecq, R.; Bozzola, C. (Jose San Martin Hosp., Buenos Aires, Argentina). *Acta Hepatogastroenterol.* 20(2):98-102, 1973.

Australia antigen (Au) and circulating antibodies were studied in 44 patients with chronic aggressive hepatitis (19 males and 25 females) and in 16 patients with chronic persistent hepatitis (9 males and 7 females). Follow-up examinations were made for 5 yr.

Controls consisted of 5 patients with primary biliary cirrhosis, 17 with acute viral hepatitis with a long incubation period, and 25 with alcoholic cirrhosis. Au was positive in 10 patients with chronic persistent hepatitis, in 20 (46%) with chronic aggressive hepatitis, and in 88% of those with acute viral hepatitis with a long incubation period, no Au was detected in any patients with alcoholic or primary biliary cirrhosis. Anti-smooth muscle antibodies occurred only in 63% of patients with chronic aggressive hepatitis, while antimitochondrial antibodies occurred in all patients with biliary cirrhosis and in 35% of those with chronic aggressive hepatitis but were absent in patients belonging to other groups; antinuclear factor was present only in 33% of the patients with chronic aggressive hepatitis. In chronic aggressive hepatitis values for the C_3 fraction of complement were normal in 48%, increased in 41%, and decreased in only 11%; immunoglobulin values were not significantly differently in Au-positive and Au-negative patients. However, mortality, systemic involvement, female sex, and the incidence of antinuclear factor were significantly more common in Au-negative patients with chronic aggressive hepatitis.

7834 ERGOMETRIC EXERCISE TOLERANCE IN PATIENTS WITH CHRONIC LIVER DISEASE. *(Ger.)*

Franken, F. H.; Wiechers, B. (St. Josef's Hosp., Wuppertal-Elberfeld, Germany). *Dtsch. Med. Wochenschr.* 98(11):528-531, 1973.

After a rest period of 1-2 weeks, exercise on the bicycle ergometer was prescribed for 7 days for 26 patients hospitalized with chronic liver disease to determine whether bed rest is really indicated for these patients. Serum bilirubin, SGOT, SGPT, alkaline phosphatase, prothrombin, and 45-min BSP retention were determined before, during, and after the exercise period. Patients had confirmed diagnoses of cirrhosis (16), chronic hepatitis (4), and fatty liver (6); 6 normal men served as controls. About 1/3 of the patients exercised for 10 min twice a day, and 2/3 exercised for 20 min twice a day. During the exercise period a significant decrease occurred in serum bilirubin, SGOT, and SGPT values in 3 patients with chronic aggressive hepatitis; liver function tests remained the same or improved slightly in all of the remaining patients with the exception of 1 who had increases in SGOT and SGPT values. This same patient subsequently developed ascites which was readily controlled with spironolactone and other diuretics. None of the patients complained of fatigue, abdominal pain, gas, or a feeling of fullness, and most claimed that they felt better after exercise. It is concluded that bed rest is only indicated for those patients with acute exacerbations of chronic liver disease.

7835 QUANTITATIVE CHANGES IN IMMUNOGLOBULINS (IgA, IgG, AND IgM) IN CHRONIC LIVER DISEASE. *(Ger.)*

Sailer, D.; Grabner, W.; Berg, G. (Med. Clin., Univ. Erlangen-Nurnberg, Erlangen, Germany). *Dtsch. Med. Wochenschr.* 98(34):1559-1563, 1973.

Serum immunoglobulin concentrations were determined by radial immunodiffusion on 50 patients with fatty liver with and without mesenchymal involvement, 14 patients with chronic aggressive hepatitis, 26 with chronic persistent hepatitis, 27 with cirrhosis, and 79 normal controls. No significant differences were found between the IgG/IgA, IgG/IgM, or IgA/IgM ratios in these groups, and no correlation was found between serum concentrations of any of the immunoglobulins and SGOT, SGPT, or serum bilirubin levels. None of the serum immunoglobulins was significantly increased in fatty liver with no mesenchymal involvement, but all 3 immunoglobulin levels were significantly increased in fatty liver with mesenchymal involvement. Only IgM levels were significantly increased in chronic persistent hepatitis, while all 3 immunoglobulin levels were significantly increased in chronic aggressive hepatitis; only IgA levels were significantly higher in chronic aggressive than in chronic persistent hepatitis. The highest serum immunoglobulin levels occurred in cirrhosis: the levels of all 3 immunoglobulins were significantly increased and were significantly higher than in any other group of patients. These results agree, for the most part, with others reported in the literature. Differences are attributed to differences in the histological, chemical, and clinical criteria used to distinguish between the various groups.

7836 THE CONCENTRATION OF SOME SERUM GLYCOPROTEINS AND SERUM IMMUNONOGLOBULINS IN CHRONIC HEPATITIS AND CIRRHOSIS. *(Ger.)*

Feher, J.; Jakab, L.; Szilvasi, I.; Papp, G. (3rd Med. Clin., Semmelweis Univ., Budapest, Hungary). *Z. Gesamte Inn. Med.* 28(14):418-420, 1973.

By using the radial immunodiffusion technique, quantitative determinations were made of ceruloplasmin, α_2-macroglobulin, β_1-C-globulin, transferrin, and immunoglobulins on serum from 10 patients with chronic persistent hepatitis, 22 with chronic aggressive hepatitis, and 18 with cirrhosis and on pooled serum from 100 blood donors. A highly significant increase in ceruloplasmin levels was found in chronic aggressive hepatitis and cirrhosis. The α_2-macroglobulin level was essentially normal in chronic persistent hepatitis and significantly increased in chronic aggressive hepatitis and cirrhosis. Concentrations of transferrin and β_1-C-globulin did not differ significantly from control values in chronic hepatitis or cirrhosis. The IgM level was significantly increased in chronic persistent hepatitis; both IgG and IgA levels were significantly increased in chronic aggressive hepatitis; and the levels of all 3 immunoglobulins, particularly those of IgA and IgM, were increased in cirrhosis. When used in conjunction with clinical, histological, and other laboratory findings, immunoglobulin determinations can be of value in the differential diagnosis of chronic liver diseases.

7837 SERUM COMPLEMENT IN CHRONIC LIVER DISEASE.

(E.) Potter, B. J.; Trueman, A. M.; Jones, E. A. (Roy. Free Hosp., London, England). *Gut* 14(6):451-456, 1973.

Total serum hemolytic complement activity (CH_{50}) and the serum concentrations of both 3rd and 4th components of the complement system (C3 and C4) were measured in 29 control subjects, 92 patients with chronic hepatocellular disease (including cryptogenic cirrhosis (30), chronic active hepatitis (22), primary biliary cirrhosis (32) and alcoholic cirrhosis (8), and 8 patients with large duct biliary tract obstruction. The mean C4 concentration was reduced in all types of chronic liver disease studied. However, mean CH_{50} and C3 values were increased in compensated primary biliary cirrhosis, were relatively normal in noncirrhotic chronic active hepatitis, and were decreased in cryptogenic cirrhosis, particularly when ascites was present. There was a significant correlation between CH_{50} and C3 in patients with chronic liver disease but no correlation between CH_{50} and C4 or between C3 and C4. Raised values for CH_{50} and C3 in primary biliary cirrhosis may be due at least in part to concomitant cholestasis since these values tend to be raised in patients with large duct biliary tract obstruction. Although primary biliary cirrhosis, chronic active hepatitis, and cryptogenic cirrhosis are considered to be a part of a spectrum of chronic liver disease associated with disturbed immunity, there are clearly definable differences between these diseases in terms of the pattern of changes in serum complement.

7838 TREATMENT OF CHRONIC AGGRESSIVE HEPATITIS WITH D-PENICILLAMINE.

(Ger.) Busse, H. J.; Nilius, R.; Otto, L.; Zipprich, B.; Eismann, R. (1st Med. Clin., Martin Luther Univ., Halle/Saale, Germany). *Z. Gesamte Inn. Med.* 28(12):178-180, 1973.

D-penicillamine was administered in increasing doses up to 1.8 g/day to 8 patients with chronic aggressive hepatitis which was progressing toward cirrhosis; these patients had failed to respond to conventional therapy and prednisone. After normalization of clinical and laboratory findings, patients were maintained on 0.9 g/day of D-penicillamine given with 60 mg/day of vitamin B_6 to prevent side effects attributed to the formation of small quantities of L-penicillamine in the body. Treatment was continued for 10-17 months in all but 2 patients who developed side effects. One patient completely lost his sense of taste 3 weeks after institution of therapy and another developed severe gastrointestinal symptoms 2 days after institution of therapy; in both cases the side effects were reversible. No other side effects were noted. D-penicillamine therapy was successful in 4 of the 6 remaining patients; relatively little improvement was observed in the other 2. Therapy decreased serum enzyme activities significantly in 4 of the 6 patients; normal levels were reached in 3. SGPT activities decreased in all 6 patients; normal levels were attained in 4. Leucine aminopeptidase activities decreased to normal values in all 6 cases. With one exception, elevated alkaline phosphatase activities returned to normal, and the albumin/globulin ratio increased in 4.

7839 SIGNIFICANCE OF IMMUNOHISTOLOGICAL FINDINGS FOR INDICATION OF IMMUNOSUPPRESSIVE THERAPY FOR CHRONIC AGGRESSIVE HEPATITIS.

(Ger.) Storch, W.; Emmrich, R.; Petzold, H. (Med. Clin., Karl Marx Univ., Leipzig, Germany). *Z. Gesamte Inn. Med.* 28(11):174-176, 1972.

Antinuclear factor (ANF), smooth muscle antibody (SMA), and mitochondrial antibody (MA) were determined by indirect immunofluorescence in sera from 25 patients with chronic aggressive hepatitis and from 25 with active cirrhosis of unknown etiology. Without taking into account the presence of Australia antigen, type of antibody, or titer, antibodies were present in 11 patients with chronic hepatitis but in only 5 with cirrhosis. In contrast to other findings reported in the literature, antibodies did not occur more frequently in women than in men. ANF and SMA were each found in 11 patients, while MA was only present in 5. Australia antigen was present in 8 of the 25 patients with chronic hepatitis and in 1 of those with cirrhosis. Antibodies were detected in 2 patients with Australia antigen: one had SMA and the other ANF. The highest titer observed was 1:640. Although autoantibodies have little or no significance in the pathogenesis of chronic active liver disease, they may be helpful in establishing whether immunosuppressive therapy is indicated in chronic hepatitis.

7840 SERUM IMMUNOGLOBULINS, COMPLEMENT COMPONENT LEVELS AND AUTOANTIBODIES IN LIVER DISEASE.

(E.) Thompson, R. A.; Carter, R.; Stokes, R. P.; Geddes, A. M.; Goodall, J. A. D. (East Birmingham Hosp., England). *Clin. Exp. Immunol.* 14(3):335-346, 1973.

Serum immunoglobulins, complement (C) component levels, and autoantibodies were measured in 117 patients (53 males and 64 females, aged 13-79 yr) diagnosed as having infective hepatitis (44), serum hepatitis (17), chronic active cirrhosis (22), micronodular (nutritional or alcoholic) cirrhosis (14), primary biliary cirrhosis (8), and extrahepatic biliary obstruction (12). All groups, except the patients suffering from extrahepatic biliary obstruction, had significantly higher IgG levels than controls, with the most marked increase (3 times control values) occurring in patients with chronic active hepatitis. IgA levels, except in patients with primary biliary cirrhosis, were also significantly higher in patients, particularly in those with micronodular cirrhosis. IgM levels were markedly elevated in patients with primary biliary cirrhosis and in those with Australian (Au) antigen-negative acute hepatitis. Of 44 antigen-negative patients, 31 had high initial IgM levels compared with only 2 of 17 antigen-positive patients. During the course of illness of antigen-negative patients, the IgM levels decreased and IgG levels increased. Serum secretory IgA was signiicantly higher in liver disease patients, particuarly in those with primary biliary cirrhosis or xtrahepatic biliary obstruction. In Au antigenositive hepatitis and chronic active hepatitis atients, C3 and C4 levels were low. The extrahepatic iliary obstruction and primary biliary cirrhosis paients had high C3 and C4 values. In patients with hronic active hepatitis, cirrhosis, and antigenositive acute hepatitis, the C6 values were low. In ll liver diseases, particularly in chronic liver amage, C7 levels were high. Weak-positive smooth uscle antibodies frequently occurred in acute hepaitis patients. Multiple autoantibodies occurred in atients with chronic active hepatitis.

841 IMMUNE PROCESSES IMPLICATED OR ASSOCIATED IN THE EVOLUTION OF CHRONIC HEPATITIS AND IRRHOSIS OF THE LIVER. *(Pol.)* Runcan, V.; Micu, D.; toica, G.; State, I. N.; Hoanca, O. (no affil.). *ed. Interna (Bucur.)* 24(6):669-676, 1972.

842 ELECTRON MICROSCOPY INVESTIGATION OF THE LYMPHOCYTES OF THE PARENCHYMA OF THE LIVER N CHRONIC POST-INFECTIOUS HEPATITIS AND CIRRHOSIS. esprozvanny, B. K.; Doronin, P. P.; Semendyaeva, . E.; Aprosina, Z. G.; Potekayeva, M. A.; Mukhin, . S. (Inst. Nutrition, Moscow, USSR). *Arkh. Patol.* 4(10):51-55, 1972.

843 IMMUNOPATHOGENESIS OF CHRONIC HEPATITIS: A REVIEW. *(E.)* Mackay, I. R.; Popper, H. Roy. Melbourne Hosp., Australia). *Aust. N.Z. J. ed.* 1(3):79-88, 1973.

844 THE DIFFERENTIATION OF CHRONIC HEPATITIS BY IMMUNOLOGICAL METHODS. *(Ger.)* Asamer, .; Judmaier, G.; Stuhlinger, W.; Platzer, S.; odisch, H. J.; Spath, P.; Huber, H. (Med. Clin., niv. Innsbruck, Austria). *Wien. Klin. Wochenschr.* 5(27-28):485-489, 1973.

845 CHANGES IN IMMUNOGLOBULINS AND HISTOLOGICAL FINDINGS WHEN CHRONIC LIVER DISEASE IS REATED WITH IMMUNOSUPPRESSANTS. *(Ger.)* Bauch, K.; uttner, W.; Lewicki, I.; Zimmermann, S.; Dempe, A. Regional Hosp., Karl Marx Stadt, Germany). *Z. esamte Inn. Med.* 28(11):169-172, 1973.

846 LONG-TERM IMMUNOSUPPRESSIVE THERAPY FOR CHRONIC AGGRESSIVE HEPATITIS. *(Ger.)* chimmelpfennig, W.; Wagner, K.; Theuer, D.; chneider, G. (2nd Med. Clin., Humboldt Univ., erlin, Germany). *Z. Gesamte Inn. Med.* 28(11): 76-178, 1973.

847 COMPLICATIONS OF IMMUNOSUPPRESSIVE THERAPY WITH CYTOSTATICS IN AUTOIMMUNE DISEASES WITH SPECIAL CONSIDERATION OF CHOLESTATIC LIVER DISEASE. *(Ger.)* Gotzel, L. (Regional Hosp., Greiz, Germany). *Z. Gesamte Inn. Med.* 28(11): 331-335, 1973.

7848 OBSERVATION OF HISTOLOGICAL CHANGES IN DRUG-INDUCED HEPATIC NECROSIS. *(Ger.)* Beckert, W. (Central Clin. Lung Dis. Tuberculosis, Bad Berka, Germany). *Z. Gesamte Inn. Med.* 28(11): 413-417, 1973.

7849 CHRONIC HEPATITIS. A RARE FORM IN FRANCE: CHRONIC ACTIVE HEPATITIS. *(Fr.)* Rautureau, J. (no affil.). *Concours Med.* 95(12):2149-2162, 1973.

7850 CLINICAL, BIOLOGIC AND MORPHOLOGIC CONFRONTATION ON THE EVOLUTIVE POSSIBILITIES OF CHRONIC HEPATITIS. *(Rum.)* Fodor, O.; Ban, A.; Nicoara, G.; Fodor, I. (3rd Med. Clin., Cluj, Rumania). *Med. Interna (Bucur.)* 24(4):687-696, 1972.

7851 CHRONIC HEPATITIDES: NOSOGRAPHIC, DIAGNOSTIC AND PROGNOSTIC ASPECTS. *(Rum.)* Hoanca, O.; Gheorghescu, B.; Russu, M.; Aposteanu, G.; Runcan, V. (Ctr. Gastroenterol., Bucharest, Rumania). *Med. Interna (Bucur.)* 24(6):677-686, 1972.

7852 AUSTRALIA ANTIGEN: PRACTICAL CONCEPTS IN INTERNAL MEDICINE. *(Fr.)* Frei, P. C. (Cantonal Hosp., Univ. Lausanne, Switzerland). *Schweiz. Med. Wochenschr.* 103(33):1170-1173, 1973.

7853 PROBLEMS ON LONG-TERM TREATMENT OF LIVER DISEASES. *(Ger.)* Renger, F.; Dokert, B. (Carl Gustav Carus Med. Acad., Dresden, Germany). *Z. Gesamte Inn. Med.* 28(11):165-168, 1973.

7854 HISTOLOGICAL AND HISTOCHEMICAL INVESTIGATIONS ON BIOPSIES IN HEPATOPATHIES. A STUDY OF THE LIVER STROMA IN CERTAIN CHRONIC HEPATITIS AND CIRRHOSIS. *(Fr.)* Miclea, C.; Litvac, E.; Schneider, F.; Tudor, L.; Dema, E.; Dinca, C.; Prodan, P. (Inst. Med., Timisoara, Romania). *Ann. Histochim.* 17(3):171-184, 1972.

See also, 6732, 6824, 7617, 7636, 7654, 7751, 7754, 7762, 7768, 7791, 7898, 7911.

Alcoholic Liver Disease

7855 RIBOFLAVIN DEFICIENCY IN COMPLICATED CHRONIC ALCOHOLISM. *(E.)* Rosenthal, W. S.; Adham, N. F.; Lopez, R.; Cooperman, J. M. (New York Med. Coll., New York). *Am. J. Clin. Nutr.* 26(8):858-860, 1973.

Riboflavin deficiency was found in 11 of 22 alcoholic patients (aged 22-69 yr) who required hospitalization for a number of complicating illnesses including acute and chronic pancreatitis, acute and chronic hepatitis, alcoholic myopathy, alcoholic liver disease, and gastrointestinal bleeding. Of these alcoholics, 5 were also heroin addicts and these 5 had biochemical evidence of riboflavin deficiency. The evidence of this deficiency was provided by increased erythrocyte glutathione reductase activity following *in vitro* addition to erythrocyte hemolysates of flavin adenine dinucleotide, a coenzyme form of riboflavin. Serum bilirubin was the only liver function test which differentiated those with riboflavin deficiency. In the deficient group the mean serum bilirubin value was 3.19 mg/100 ml, compared with 1.26 mg/100 ml for the normal group. The biochemical abnormality, which was not accompanied by the classical physical findings of riboflavin deficiency, was corrected within 2 to 7 days by riboflavin administration. This sensitive and easily performed test can be used to evaluate previously unsuspected riboflavin deficiency in a variety of clinical conditions.

7856 SUBCELLULAR FEATURES OF ALCOHOLIC LIVER LESION: ALCOHOLIC HYALIN. *(E.)* Horvath, E.; Kovacs, K.; Ross, R. C. (St. Michael's Hosp., Toronto, Canada). *J. Pathol.* 110(3):245-250, 1973.

Liver biopsies obtained from 16 chronic alcoholics were used to study the fine structure and fate of Mallory bodies (alcoholic hyaline). Alcoholic hyalin was detected in the form of 3 ultrastructurally distinguishable varieties of well-defined fibrillar material. It was never membrane-bounded or taken up by cytosegresomes in the hepatocytes. Its morphology was unchanged in foci of satellitosis, even when the cellular organelles were destroyed. Alcoholic hyalin has been consistently associated with rough endoplasmic reticulum and free ribosomes in the hepatocytes. It is suggested that an unknown metabolic defect causes protein to be deposited at the site of synthesis and this represents alcoholic hyalin. It is suggested that decreased elimination of protein products, rather than enhanced protein synthesis, may be involved in this process.

7857 INHIBITION BY NICOTINIC ACID OF HEPATIC STEATOSIS AND ALCOHOL DEHYDROGENASE IN ETHANOL-TREATED RATS. *(E.)* Baker, H.; Luisada Opper, A.; Sorrell, M. F.; Thomson, A. D.; Frank, O. (New Jersey Med. Sch., East Orange). *Exp. Mol. Pathol.* 19(1):106-112, 1973.

A single intoxicating dose of ethanol (6.0 g/kg p.o. through a stomach tube) reduced the ratio of nicotinamide adenine dinucleotide (NAD) to reduced NAD and increased the ratio of reduced nicotinamide adenine dinucleotide phosphate to nicotinamide adenine dinucleotide phosphate in the liver of male Sprague-Dawley rats. Administration of nicotinic acid (250 mg/kg p.o. through a stomach tube) prevented accumulation of nonesterified fatty acid, total fats, and neutral fats in the liver of rats given ethanol and kept blood ethanol levels elevated. It is suggested that nicotinic acid acts by blocking ethanol oxidation, probably by inhibiting alcohol dehydrogenese, a mediator of the principal oxidative pathway of ethanol metabolism. It was inferred that nicotinic acid inhibits the enzyme by binding at the adenosine diphosphate ribose site since addition of Zn^{++} *in vitro* failed to reverse inhibition of alcohol dehydrogenase by nicotinic acid. Blockage at this site would prevent coenzyme (NAD) from binding to apoenzyme and result in a block in ethanol oxidation.

7858 GAS-CHROMATOGRAPHIC-MASS-SPECTROMETRIC DETERMINATION OF URINARY ACID PROFILES OF NORMAL YOUNG ADULTS. II. THE EFFECT OF ETHANOL. *(E.)* Witten, T. A.; Levine, S. P.; Killian, M. T.; Boyle, P. J. R.; Markey, S. P. (VA Hosp., Denver, Col.). *Clin. Chem.* 19(9):963-966, 1973.

Urinary acid metabolic profiles of 26 healthy young adults (16 males and 10 females, aged 21-29 yr) who were maintained on a palatable standard diet for 3 days have been studied by combined gas chromatography-mass spectrometry. Means and standard deviations of the excretion rates of individual, identified acids were determined 5 hr after the ingestion of ethanol (1.2 g/kg, over a 30 min period) and compared with basal values previously reported. A significant net effect of ethanol was demonstrated for only 6 of the acids studied: α- and β-hydroxybutyric, adipic, β-methyladipic, p-hydroxyphenylacetic, and 2,5-furandicarboxylic acids. Urinary acids showing no net ethanol-induced excretion rate change were β-hydroxyisovaleric, succinic, 5-hydroxymethyl-2-furoic, tartaric, and dihydroxyphenylpropionic acids.

7859 ACUTE ALCOHOLIC HEPATITIS IN SINGAPORE: A COMPARISON WITH WESTERN SERIES. *(E.)* Fung, W. P.; Tan, K. K.; Tye, C. Y. (Fac. Med., Univ. Singapore). *Aust. N.Z. J. Med.* 3(3):272-278, 1973.

A Singapore series of 50 cases of acute alcoholic hepatitis found in a 3 yr period was compared with 2 western series. Clinical jaundice, hepatic coma, and deaths were significantly more frequent in the Singapore than in the western series. A significantly higher incidence of hypokalemia was probably responsible for the higher incidence of hepatic coma in the Singapore series. Macrocytic anemia was the

mmonest anemia in the western series but was not
und in the Singapore series, in which hypochromic
emia was the commonest. The SGPT level was more
equently raised in Singapore patients. However,
rum transaminase levels were normal in some cases
acute alcoholic hepatitis in both Singapore and
stern series. It is concluded that serum trans-
inase levels are not reliable in diagnosing acute
coholic hepatitis. A liver biopsy is essential
a firm diagnosis. The incidence of cirrhosis
the Singapore series was significantly higher than
t of one western series, but lower than that of
other. The incidence of Mallory's hyaline in
Singapore series was lower than the western
ies because it was not essential for diagnosis
the Singapore patients. Besides these few diff-
nces, acute alcoholic hepatitis was fairly simi-
in Singapore and western countries.

0 EFFECT OF MEDIUM-CHAIN TRIGLYCERIDES ON LIVER FATTY ACID COMPOSITION IN ALCOHOLICS
H OR WITHOUT CIRRHOSIS. *(E.)* Malagelada, J. R.;
scheer, W. G.; Houtsmuller, U. M.; Vergroesen, A.
Shah, M.; Iber, F. L. (VA Hosp., Syracuse, N.Y.).
J. Clin. Nutr. 26(7):738-743, 1973.

fatty acid composition of liver biopsies from 7
ients with alcoholic cirrhosis fed a normal hospital
t (100 g fat for 2 weeks) was compared with that of
cirrhotic alcoholics (6 patients) on the same diet.
mitic (16:0), stearic (18:0), oleic (18:1), and
oleic (18:2) acids accounted for more than 70% of
al liver fatty acids in both groups. No signifi-
t difference was found in the relative amounts of
of 14 fatty acids ranging from $C_{12:0}$ to $C_{22:6}$.
stitution of medium-chain triglycerides for long-
in triglycerides for 2 weeks in similarly selected
oholics with and without cirrhosis changed the
er lipid composition of cirrhotics (6 patients) but
no effect on that of alcoholics without cirrhosis
patients). Shorter chain fatty acids ($C_{14:0}$ and
$_{:0}$) increased and long-chain fatty acids ($C_{18:0}$
$C_{18:1}$) decreased. It is probable that persistently
vated serum levels of medium-chain fatty acids
nd in cirrhotics was responsible for the shift
ard shorter chain fatty acids. Serum albumin
els below 3.5 mg/100 ml were found in 22 of the
alcoholics (13 with cirrhosis) selected for the
dy. No change occurred in the 2 groups of the
g-chain triglyceride diet, but serum albumin levels
reased significantly in patients fed medium-chain
glycerides for 2 weeks. This suggests that paren-
al function is improving. These findings imply
t medium-chain triglycerides are of potential value
the treatment of cirrhosis.

1 MILD CLINICAL FORMS OF ACUTE ALCOHOLIC LIVER DISEASE: SIGNIFICANCE AND DIFFEREN-
L DIAGNOSIS. *(Ger.)* Linhart, P.; Kommerell, B.;
eschild, N. (Med. Clin., Univ. Heidelberg, Germany).
ch. Med. Wochenschr. 98(19):983-988, 1973.

omputer analysis of the histories and clinical, biochemical, and histological findings in 500 patients with liver disease showed that mild forms of acute alcoholic liver disease had been undiagnosed in 14 cases. These patients (13 men and 1 woman, aged 27-55 yr) had been hospitalized for 11-27 days. Their average alcohol consumption was 50-100 g/day in 5 cases and more than 100 g/day in 9. Drugs (amitriptyline and phenylbutazone, resp.) could be implicated in only 2 cases, and only 2 patients had associated diseases (acute diffuse glomerular nephritis and mild diabetes mellitus, resp.). None of the patients was malnourished and only one had a fever. The liver was palpable in 10 and painful when subjected to pressure in 6. Eight patients had jaundice but none had ascites, skin signs suggestive of parenchymal liver disease, or an elevated WBC. The erythrocyte sedimentation rate was increased in 7, and the Quick time was decreased to less than 50% in 2. Two patients with symptoms of Zieve's syndrome were anemic. Serum immunoglobulins and albumin were within the normal range in all 14 cases. SGOT and SGPT were increased in all 114 patients, and LDH was slightly increased in most. Alkaline phosphatase activities were increased and/or lipoprotein X was present in 9 of the 10 patients with cholestasis; 2 of these 10 patients were anicteric while the rest had bilirubin levels of 2.8-12.5 mg/100 ml. Only 1 patient with jaundice had no evidence of cholestasis. Liver biopsies showed that fatty liver was present in 11, fibrosis in 12, Kupffer cell proliferation in 3, and inflammatory infiltration of the periportal fields in 7. The importance of correctly diagnosing mild forms of alcoholic liver disease is emphasized since clinical and histological changes are reversible if patients abstain from alcohol.

7862 THE NATURAL HISTORY OF ESOPHAGEAL VARICES IN PATIENTS WITH ALCOHOLIC LIVER CIRRHOSIS. AN ENDOSCOPIC AND CLINICAL STUDY.

(E.) Dagradi, A. E. (Long Beach VA Hosp., Calif.). *Am. J. Gastroenterol.* 57(6):520-540, 1972.

A comparison was made of 15 chronic alcoholics (all men, aged 25-68 yr) with large and extensive esophageal varices who discontinued further ingestion of alcohol and a similar group of patients who continued the habit. The patients in the former group were followed from 9 to 83 months; those in the latter group, from 4 to 38 months. Histologic proof of advanced liver cirrhosis was present in all cases. in 80% of patients who discontinued drinking, a significant reduction occurred in the caliber and in the extent of the esophageal varices. Progressive enlargement of the 4+ to 5+ varices occurred in 65% of the group who continued the habit. Rupture of esophageal varices did not occur in any patient in the former group and all were olive at the conclusion of this study. Massive bleeding from ruptured varices occurred in 8 patients in the latter group; 9 died during the period of observation. A significant reduction in the degree of hepatomegaly, absence of recurrence of ascites, and marked improvement in the total bilirubin level and in the albumin/globulin ratio occurred in the group which stopped drinking, while further deterioration in these parameters was observed in the group who continued. The caliber and extent of even the most highly developed esophageal varices is reversible in many patients with alcoholic cirrhosis who stop drinking. The rather benign clinical course which they subsequently follow, and their markedly improved survival, emphasizes the critical importance of permanent and total abstinence from further use of alcohol. The attainment of this objective must be a prime consideration in the management of patients with this disorder.

7863 EARLY DIAGNOSIS OF ALCOHOLIC CIRRHOSIS. *(Fr.)* Aron, E.; Lamy, J. N.; Weill, J. D. (Fac. Med., Tours, France). *Ann. Gastroenterol. Hepatol. (Paris)* 9(1):1-17, 1973.

7864 CARBOHYDRATE TOLERANCE AND INSULIN SECRETION IN PATIENTS WITH FATTY LIVER. *(Ger.)* Hausmann, L.; Schubotz, R.; Born, H.; Kaffarnik, H. (Med. Polyclin., Univ. Marburg, Germany). *Schweiz. Med. Wochenschr.* 103(28):1002-1007, 1973.

7865 FEATURES OF ALCOHOLIC HEPATITIS. *(Ger.)* Schnack, H. (Wilhelminenspital, Vienna, Austria). *Dtsch. Med. Wochenschr.* 98(12):625-627, 1973.

7866 ZIEVE'S SYNDROME. (REPORT OF 2 CASES). *(Fr.)* Sudre, Y.; d'Eyzac, A. T.; Becq Giraudon, B. (Intern. Med. Serv., Poitiers, France). *Sem. Hop. Paris* 49(12):849-858, 1973.

See also, 6481, 6494, 6499, 6510, 6742, 7882, 7903.

LIVER AND BILIARY TRACT

Cirrhosis

7867 INHIBITION OF PHA-STIMULATED LYMPHOCYTE TRANSFORMATION BY PLASMA FROM PATIENTS WITH ADVANCED ALCOHOLIC CIRRHOSIS. *(Fr.)* Hsu, C. S.; Leevy, C. M. (New Jersey Coll. Med. Dent., Newark). *Med. Chir. Dig.* 2(1):9-11, 1973.

Lymphocyte culture studies in liver diseases revealed that the plasma from patients with advanced alcoholic cirrhosis (9 cases) contained factor(s) which suppresses the normal lymphocyte response to phytohemagglutinin from 170% ± 63% to 17% ± 10%. This inhibiting effect was destroyed by heating the plasma at 56°C for 60 min, thus indicating the inhibition was due to certain heat-labile factor(s). A similar blocking factor was also noted in plasma from patients with allergic rhinitis (5), granulomatous hepatitis (1), uremia (1) and carcinomatosis (1) but not in obstructive jaundice (2 cases). The magnitude of blocking effects in all of these conditions was correlated with serum γ-globulin levels. The finding of plasma inhibitory factors in 4 patients with allergic rhinitis suggests an increase in immunoregulatory humoral factor may occur.

7868 EXTRAHEPATIC PORTAL HYPERTENSION IN CHILDREN. *(E.)* Myers, N. A.; Robinson, M. J. (Roy. Children's Hosp., Melbourne, Australia). *J. Pediatr. Surg.* 8(4):467-473, 1973.

In a 20-yr period, gastrointestinal bleeding was by far the most common presenting symptom and was seen in 30 of 54 children (30 boys and 24 girls), aged under 1 yr to 14 yr) with portal hypertension caused by cavernous transformation of the portal vein. In 20 cases children presented with asymptomatic splenomegaly. Associated diseases consisted of cirrhosis (18 cases), viral hepatitis (8), cystic fibrosis of the pancreas (4), biliary atresia (4), glycogen storage disease (1), Wilson's disease (1) malignant hepatoma (3), intrahepatic venous thrombosis secondary to hamartoma (1), and congenital anomaly of the inferior mesenteric vein (1). Liver function tests were normal in all cases. The patients were classified into 4 groups according to the primary surgical procedure employed: (1) no surgical treatment (17 cases); splenectomy alone (4 cases); (3) direct attack on the bleeding area, e.g. by ligation of varices, portaazygos disconnection, or esophagogastrectomy (21 cases); or (4) shunt surgery (12 cases). Of the patients who received no surgical treatment, all are alive and well. Although only 4 of these 17 patients presented with severe gastrointestinal bleeding, another 4 had at least one major bleeding episode later. Of the 37 children who underwent surgery, many developed postoperative bleeding and had to undergo further surgery. There were 7 deaths: 1 followed splenectomy, 4 a direct attack on the bleeding area, and 2 occurred after shunt surgery; 1 patient died of unrelated causes. Surgery is not recommended in children under 4 yr old or during acute bleeding episodes. A portosystemic shunt is indicated for recurrent life-threatening bleeding.

7869 CLOTTING DISORDER IN CIRRHOSIS. CLINICAL AND CLINICAL CHEMICAL OBSERVATIONS. *(Ger.)*

Bungert, H. J.; Leonhardt, H. (Steglitz Clin., Free Univ., Berlin, Germany). *Med. Klin.* 67(16):578-586, 1972.

Coagulation status was investigated in 28 patients (20 men and 8 women, aged 32-68 yr) with decompensated cirrhosis. Patients were divided into 3 categories: (1) 11 with pronounced esophageal varices; (2) 6 with bleeding varices; and (3) 11 with little or no evidence of varices. A correlation was found between the extent of esophageal varices and latent consumption coagulopathy (disseminated intravascular coagulation) which is defined as hypofibrinogenemia, thrombocytopenia, and a decrease in the maximum amplitude of the thromboelastogram. Scintigraphy of the liver and spleen suggest that decreased fibrinogen levels and thrombocytopenia may be due to phagocytosis of platelets and fibrin particles by cells in the reticuloendothelial system of the spleen and liver. Reduced antiplasminogen production and the production of fibrinolytic substances by the liver may also account for reduced fibrinogen levels. The relatively small increase in blood ammonia levels in group (1) is attributed to effective collateral circulation and peripheral detoxification, while the much higher blood ammonia levels in group (3) are attributed to reduced collateral blood flow which was demonstrated by splenic portography. Increasing stasis eventually disturbs the equilibrium between hyper- and hypocoagulation and this can result in variceal bleeding. It is postulated that latent consumption coagulopathy is causally related to reduced collateral blood flow. From these findings, it is concluded that blood ammonia and fibrinogen concentrations and platelet and reticulocyte counts are indirect criteria for evaluating blood flow in the collateral circulation.

7870 INDICATIONS FOR AND RESULTS FROM SCLEROSING THERAPY IN ESOPHAGEAL VARICES. *(Ger.)*

Paquet, K. J. (Surg. Clin., Univ. Bonn, Germany). *Therapiewoche* 22(34):2622-2628, 1972.

In a 3-yr period, sclerosing therapy was administered to 48 patients with bleeding esophageal varices. In 21 cases, sclerosing therapy was given during acute variceal bleeding to 14 patients with decompensated cirrhosis or hepatic precoma, 4 with thrombosed shunts, and 3 with prehepatic block and no blood vessels that could be anastomosed. Using a special magnifying esophagoscope, 2 ml of sclerosing agent (5% Varicocid or Dondrene) was injected at various sites in the mucosa next to the varices; the total quantity injected was 10-15 ml. Several sessions were given at 3-5-day intervals. Nine of these 21 patients died of hepatic coma and recurrent bleeding (5 cases), bleeding from gastric varices (2), myocardial infarction and an aneurysm in the wall of the heart (1), and esophageal necrosis and pyothorax on the right (1). Of 27 patients treated during intervals between bleeding, 16 had decompensated cirrhosis or hepatic precoma, 9 had thrombosed shunts or no blood vessels that could be anastomosed, and 2 had developed portal thrombosis after splenectomy. Ten of these 27 patients died of hepatic coma (7 cases), bleeding from gastric varices (2), and bleeding from a stress ulcer (1). Thirty patients survived 3 months to 3 yr after sclerosing therapy. In about 1/3 of the cirrhotics it was later possible to treat portal hypertension by shunt surgery. Bleeding of gastric varices in a complication of this technique resulting from an increase in pressure in these varices, and esophageal necrosis with pyothorax results from injecting sclerosing agent into the tunica muscularis of the esophagus. This technique cannot be used in the treatment of gastric varices.

7871 NEW ASPECTS OF THE PATHOGENESIS OF ASCITES IN CIRRHOSIS AS SEEN WITH LAPAROSCOPY.

(Ger.) Krohl, R.; Leuschner, U. (Ctr. Internal Med., Johann Wolfgang Goethe Univ., Frankfurt/Main, Germany). *Z. Gastroenterol.* 10(6):429-432, 1972.

In cirrhosis, even mild portal hypertension reduces or eliminates reabsorption of lymph in the distal part of hepatic sinusoids and results in a passive increase in lymph production. Subcapsular lymphangiectases and small lymph cysts form which allow lymph to escape because of their extremely high permeability to protein or burst because of the high presures (up to 6 cm H_2O) inside the cysts. The protein concentration in lymph was 80-90% lower than that in the blood. Lymph contained almost the same protein fractions as blood, but in 5 cases γ-globulin and IgG were higher than in serum, suggesting that immunoglobulins are synthesized in the liver by plasma cells and are transported by lymphatics in the liver. Transaminase activities were 20-30% higher in lymph than in serum. Hypoalbuminemia, which is present in severe parenchymal damage, reduces the colloid osmotic pressure in the distal part of the sinusoids and limits or prevents reabsorption of primary lymph. The decrease in circulating blood volume associated with ascites activates aldosterone production, but steroid catabolism is reduced in the damaged liver. The resulting secondary hyperaldosteronism increases sodium and water retention and potassium loss, and thus promotes ascites, but it is not a causative factor.

7872 HEPATIC ARTERIAL ESCAPE FROM VASOPRESSIN-INDUCED VASOCONSTRICTION: AN ANGIOGRAPHIC INVESTIGATION. *(E.)* Conn, H. O.; Ramsby, G. R.; Storer, E. H. (Yale Univ. Sch. Med., New Haven, Conn.). *Am. J. Roentgenol. Radium Ther. Nucl. Med.* 119(1): 102-108, 1973.

The effect of vasopressin on the common hepatic, gastroduodenal, left gastric, splenic, and superior mesenteric arterial systems was studied in 15 patients who received celiac axis angiography and in 8 who received superior mesenteric arteriography. Arteries less than 6 mm in diameter were increasingly responsive to the intra-arterial administration of vasopressin as their size diminished, whereas arteries less than 1 mm in diameter often became invisible during vasopressin administration as larger arteries in the same arterial system constricted. Hepatic arteries showed a moderate degree of dilatation. Superior mesenteric arteries, splenic arteries, gastroduodenal and left gastric arteries all responded with vasoconstriction. The small mean increment in diameter of the hepatic arteries of 7.7% resulted in a 34% increase in blood flow. Gastroduodenal arterial blood flow was decreased to 25% of the pre-vasopressin level due to a decrease in mean diameter of the arteries of 29.2%. It is suggested that vasopressin may be used in exploring the derangements of portal hypertension.

7873 DUODENAL VARICES WITH CIRRHOSIS OF THE LIVER: REPORT OF THREE CASES. *(E.)* Hellstrom, H. R.; Horvat, B. L.; McCoy, M. M. (Univ. Pittsburgh, Sch. Med., Pa.). *Am. Surg.* 39(9):518-521, 1973.

Case reports are presented for 3 men, aged 44-55 yr, with massive upper gastrointestinal bleeding and histories of cirrhosis dating back 3-10 yr. Submucosal varices were found at autopsy in the second and third portions of the duodenum in 2 patients. In the third patient submucosal varices were detected in the distal duodenum and contiguous jejunum at exploratory laparotomy. This patient died of a myocardial infarction 8 days after excision of the varices. It is suggested that duodenal varices may be a more common cause of upper gastrointestinal bleeding in patients with portal hypertension. This diagnosis should be considered in patients in whom tamponade therapy failed to stop bleeding; this occurred in 2 of the 3 patients described here.

7874 HEPATIC EXTRACTION AND CLEARANCE OF RENIN IN CIRRHOSIS. *(Ger.)* Wernze, H.; Seki, A.; Schneider, K. W.; Jesse, R. (Med. Clin., Univ. Wurzburg, Germany). *Klin. Wochenschr.* 50(6):302-310, 1972.

Renin activity was determined in arterial blood and blood obtained by catheterization of the hepatic vein in 14 patients with compensated and 8 patients with decompensated cirrhosis; 20 patients with various types of hypertension served as controls. The calculated hepatic renin extraction was not decreased, but individual values varied over a wide range. In compensated cirrhosis the mean hepatic renin extraction was 17.8 ± 17.3%, and the hepatic renin clearance was decreased to 68% of control values. In the decompensated group the hepatic renin extraction was 30.5 ± 5.8%, and hepatic renin clearance was decreased to 42.5% of control values. The increase in arterial angiotensin values was highly significant in both groups of cirrhotics. Thus, elevated plasma renin activity in progressive cirrhosis can be explained by an increase in renal secretion combined with a decrease in hepatic renin extraction. No significant correlation was found between hepatic renin extraction and wedged hepatic vein pressure or hepatic plasma flow (indocyanine green method). It is hypothesized that hepatic extraction of renin is affected by the prolonged intrahepatic passage time in cirrhosis.

7875 BILE CANALICULAR ANTIBODY IN PRIMARY BILIARY CIRRHOSIS AND IN OTHER LIVER DISEASES. *(E.)* MacSween, R. N. M.; Armstrong, E. M.; Gray, K. G.; Mason, M. (Western Infirm., Glasgow, Scotland). *Lancet* (7817):1419-1421, 1973.

Sera from 111 patients with a diagnosis of primary biliary cirrhosis and from 198 additional patients with various other liver diseases were examined. Using rabbit liver as substrate, antibody directed against bile canaliculi was demonstrated in the serum of 39 primary biliary cirrhosis patients. In 26 (23%) of the primary biliary cirrhosis sera, canalicular antibody was found alone and in a further 13 (12%) it occurred concurrently with smooth-muscle antibody. In patients with other liver diseases, canalicular antibody was found in 43 of 198 (23%) serum samples. The diagnoses in these seropositive patients were: acute hepatitis (15), cryptogenic cirrhosis (7), chronic active hepatitis (3), primary biliary cirrhosis (3), and miscellaneous (15). Of the 15 acute hepatitis patients, canalicular antibody occurred concurrently with smooth-muscle antibody. Results indicate that, at least in some cases, the canalicular antibody is clearly distinct from smooth-muscle antibody. The antibody has been shown to react also with human bile canaliculi, and thus it might represent a possible organ-specific marker of acute and chronic liver disease.

7876 STUDIES ON PRIMARY BILIARY CIRRHOSIS IN CHILDREN. *(Ger.)* Luders, D.; Brunner, G. (Pediatric Clin., Univ. Gottingen, Germany). *Monatsschr. Kinderheilkd.* 121(7)321-323, 1973.

The first case of primary biliary cirrhosis in a chil is reported. A 6-week-old girl developed jaundice, light-colored stools, and increased IgM levels. Antimitochondrial antibody, present in a titer of 1:64 in serum, was also detected by immunofluorescence in the walls of intrahepatic bile ducts and in the epithelium of a few periportal ductules. Serum phosphatides, triglycerides, bile acids, the erythrocyte sedimentation rate, and serum complement were increased; no Australia antigen was detected. Two laparotomies failed to show any evidence of extrahepatic biliary obstruction. A liver biopsy taken at age 6 months showed changes characteristic of intrahepatic cholestasis, but no signs of cirrhosis were evident. A second biopsy taken at age 3 yr revealed degenerative changes characteristic of primary biliary cirrhosis. The child has had pruritis, and 3 spontaneous bone factures resulting from osteoporsis but no xanthomas or esophageal varices. Symptomatic therapy has not been too successful. Administration of 25-hydroxycholecalciferol p.o. helped to consolidate a fracture, but a second spontaneous fracture occurred during therapy. The second fracture healed satisfactorily with vitamin D_3 administered i.m. Cholestyramine produced a slight improvement in the pruritis, but very large doses were necessary. Both pruritis and hyperbilirubinemia responded to a 14-day course of phenobarbital. Because of the life-threatening nature of primary biliary cirrhosis, the patient is being treated with azathioprine; it has relieved pruritis and reduced alkaline phosphatase activities, but has had no effect on titers of antimitochondrial antibody.

7877 CONTROL OF VARICEAL BLEEDING BY SUPERIOR MESENTERIC ARTERY PITRESSIN PERFUSIONS-COMPLICATIONS AND INDICATIONS.

(E.) Marubbio, Jr., A. T.; Lombardo, R. P.; Holt, P. R. (Hennepin County Gen. Hosp., Minneapolis, Minn.). *Am. J. Dig. Dis.* 18(7):539-543, 1973.

This report describes 18 continuous perfusions of the superior mesenteric artery with Pitressin in a group of 9 unselected patients (7 males and 2 females, aged 23-72 yr) with severe cirrhosis of the liver and proven bleeding from esophageal varices. Pitressin perfusion at 0.3 U/min for 20 min alternating with 0.15 U/min for 20 min rapidly stopped the bleeding in all patients, but rebleeding occurred 1 hr to 4 days after the drug was discontinued. This procedure was most useful in controlling massive variceal hemorrhage, allowing time for selection and preparation of patients for semi-emergency surgical portasystemic shunting while maintaining hepatic blood flow and preventing hepatic decompensation. Several problems related to mesenteric arterial cannulation were encountered. Moreover, perfusion of Pitressin for greater than 24 hr caused problems in free water clearance. In 2 patients in whom vasopressin tannate was perfused during surgery to reduce bleeding, the tissues were extraordinarily edematous, and both patients developed pulmonary ventilation problems after surgery. In 1 of these, an adult respiratory distress syndrome caused death postoperatively.

7878 THE PRESENTATION AND DIAGNOSIS OF 100 PATIENTS WITH PRIMARY BILIARY CIRRHOSIS.

(E.) Sherlock, S.; Scheuer, P. J. (Roy. Free Hosp., London, England). *N. Engl. J. Med.* 289(13): 674-678, 1973.

In a 7 yr period primary biliary cirrhosis was diagnosed in 100 patients (90 females and 10 males, aged 32-72 yr). In 57 cases the disease presented as pruritus without jaundice. In 27 cases the jaundice was delayed for 1-20 yr after the start of pruritus. Pruritus appeared in 5 cases during pregnancy and was confused with cholestatic jaundice of the last trimester. Hepatosplenomegaly caused the initial study in 3 patients in whom primary biliary cirrhosis was noted. Portal hypertension was the presenting symptom in 4 cases, 3 with bleeding esophageal varices and 1 with ascites. Diagnosis was made during investigation of other conditions in 4 patients, duodenal ulcer, dermatomyositis, rheumatoid arthritis, and the sicca syndrome. Associated diseases apart from those mentioned above included rheumatoid arthritis (5), ulcerative colitis (1), autoimmune thyroiditis (6), the sicca syndrome (3), Raynaud's phenomenon (1), and renal tubular acidosis (1). Serum bilirubin ranged from less than 2 mg/100 ml in 41% to over 10 mg/100 ml in 6%. Serum alkaline phosphatase concentrations exceeded 70 King-Armstrong U in 47 cases. Of 41 operative biopsies in this series, 28 (70%) were diagnostic and 13 were compatible with primary biliary cirrhosis. Of the pathognomonic ones, 6 showed granulomas. Of 59 needle biopsies, 17 (29%) were diagnostic, 3 showing granulomas; the remaining 42 (71%) were compatible with primary biliary cirrhosis.

7879 EFFECT OF INCREASED INTRAABDOMINAL PRESSURE ON HEPATIC HEMODYNAMICS IN PATIENTS WITH CHRONIC LIVER DISEASE AND PORTAL HYPERTENSION.

(E.) Iwatsuki, S.; Reynolds, T. B. (Univ. Southern California, Sch. Med., Los Angeles). *Gastroenterology* 65(2):294-299, 1973.

Measurements of wedged hepatic vein pressure, abdominal inferior vena caval pressure, and right atrial pressure were made on 15 patients with alcoholic cirrhosis during hepatic vein catheterization for evaluation of portal hypertension. Measurements were made before and after paracentesis in 5 patients and before and after injection of air into the peritoneal cavity in 10. Hepatic blood flow was estimated by fractional clearance of indocyanine green in 5 patients before and after pneumoperitoneum. The gradient between wedged hepatic vein pressure and right atrial pressure was dependent upon the intraabdominal pressure, but the gradient between wedged hepatic vein pressure and abdominal vena caval pressure was independent of the intraabdominal pressure. Consequently, wedged hepatic vein pressure is a meaningful measure of the resistance to flow through the liver in tense ascites only if it is corrected for the high intraabdominal pressure. Both hepatic flow and the extraction rate of indocyanine green were sometimes changed by high intraabdominal pressure, but the direction of change was not uniform and the mean change was not significant. This finding, together with theoretical considerations, makes it unlikely that blood flow in esophageal varices is increased by high intraabdominal pressure. Thus, paracentesis is probably not useful in the treatment of bleeding esophageal varices.

7880 URIDINE DIPHOSPHATE GLUCOSE IN CIRRHOTIC PROCESSES. *(Sp.)* Betancor Leon, P. (Francisco Franco Provincial Munic. Sanit., Barcelona, Spain). *Rev. Esp. Enferm. Apar. Dig.* 39(4):463-478, 1973.

Uridine diphosphate glucose (UDPG; 20 mg i.m. every 12 hr) was given for 30 days to 32 cirrhotics, aged 25-71 yr; 3 patients died during the first few days of treatment and are not included. Of these 29 patients, 7 had posthepatitic cirrhosis, 2 had porphyric cirrhosis, and 20 had septal cirrhosis; most of the patients were alcoholic and 3 were positive for Australia antigen. Symptoms included jaundice (27), ascites (18), collateral circulation (19), oliguria (15), palmar erythema (13), spider nevi (23), Dupuytren's contracture (9), hepatomegaly (24), splenomegaly (15), and esophageal varices (8). After 30 days of treatment, mean serum bilirubin concentrations had decreased to 2.44 mg/100 ml from 4.70 mg/100 ml before treatment. No significant changes occurred in prothrombin activity, plasma albumin levels, or BSP retention. Since diuresis increased significantly in patients with severe ascites who received a similar diet, the effect of UDPG on diuresis could not be established. Urinary sodium excretion increased and potassium loss decreased significantly. For the best results, it is recommended that UDPG be combined with small doses of diuretics and vitamin supplements when they are indicated.

7881 ELECTRON MICROSCOPIC STUDY OF THE DISTRIBUTION OF THE AUSTRALIA ANTIGEN IN INDIVIDUAL SERA OF 50 SEROLOGICALLY POSITIVE BLOOD DONORS AND TWO PATIENTS WITH SERUM HEPATITIS. *(E.)* Stannard, L. M.; Moodie, J.; Keen, G. A.; Kipps, A. (Univ. Cape Town Med. Sch., South Africa). *J. Clin. Pathol.* 26(5):209-216, 1973.

Electron microscopy showed the presence of Australia antigen particles in 47 of 50 plasma samples from blood donors selected for study on the basis of a positive serological test for this antigen. The antigen was present in amounts ranging from a few scattered 20 nm spherical particles to vast quantities of antigen comprising 20 nm spheres, tubules, and 42 nm Dane particles in varying proportion. Antigen-antibody complexes were present in 50% of the plasma samples; in the other 50% the antigen had a random distribution. Incidence of Dane particles was 30%. No common pattern of antigen distribution was seen in the plasma samples from 3 donors who had been implicated in the transmission of serum hepatitis. Serial serum samples from 2 patients with serum hepatitis showed small spheres as aggregates; Dane particles were seen in the samples in only 1 of the patients. In both patients the Australia antigen was cleared from the blood by a phenomenon that was presumed to be evidence of a normal immune response. The role of persistent antigen in the blood of the chronic carriers is still uncertain; but careful evaluation is deemed important because of the high incidence of Dane particles and immune complexes, both of which may participate in the pathogenesis of tissue damage.

7882 CLINICAL COMPARISON OF THE END-TO-SIDE AND SIDE-TO-SIDE PORTACAVAL SHUNT: TEN YEAR FOLLOW-UP. *(E.)* Iwatsuki, S.; Mikkelsen, W. P.; Redeker, A. G.; Reynolds, T. B.; Turrill, F. L. (Univ. Southern California Sch. Med., Los Angeles). *Ann. Surg.* 178(1):65-69, 1973.

Two groups of 40 patients received end-to-side or side-to-side portacaval shunt for the treatment of portal hypertension between 1959 and 1962 and have been followed since that time. The choice of shunt was based on anatomic factors found at operation. The groups were comparable in regard to age, sex, type of disease, preoperative liver function, and duration of operation. Survival has been essentially equal in the 2 groups, with nearly 50% of the patients alive 5 years and 20% alive 10 years postoperatively. Severe hepatic encephalopathy developed in 10 patients with side-to-side shunt and in 4 end-to-side shunt. Encephalopathy appeared for the first time as long as 5 years after operation. All 14 patients with severe encephalopathy have died, in most instances from hepatic failure. In all other respects, the results of the 2 types of shunts seem similar.

7883 A RATIONAL APPROACH TO THE HEPATORENAL SYNDROME. *(E.)* Conn, H. O. (VA Hosp., West Haven, Conn.). *Gastroenterology* 65(2):321-340, 1973.

In the hepatorenal syndrome patients with decompensated cirrhosis develop acquired, functional renal failure in which none of the usual causes of renal insufficiency are present and in which the kidneys themselves are normal. The disorder stubbornly resists attempts to improve renal function and usually ends in death. The syndrome occurs almost invariably in cirrhotic patients, usually alcoholic, the great majority of whom have decompensated liver disease characterized by jaundice, hepatosplenomegaly, hypoalbuminemia, and portal hypertension. The recently demonstrated reversibility of functional renal failure which characterizes the hepatorenal syndrome appears to be a key to the mysteries of the syndrome and permits rational treatment for the first time. In therapy it is essential first to exclude prerenal azotemia which may completely mimic the syndrome. Next it is necessary to empirically expand the plasma volume to determine if expansion of the total plasma volume will increase glomerular filtration. Reduction of intraabdominal pressure by paracentesis may improve the altered renal hemodynamics. If these measures are inadequate, treatment with dilute infusion of phenylalanine-lysine vasopressin may be tried or portacaval anastomosis (in patients whose liver function will tolerate major surgery) may be considered. Adrenocortical steroid therapy may be used. As a last resort dibenzyline, metaraminol, L-dopa or other agents that have occasionally been reported to be beneficial may be tried.

7884 THE EFFECT OF MEDIUM-CHAIN TRIGLYCERIDE ON ^{47}CALCIUM ABSORPTION IN PATIENTS WITH PRIMARY BILIARY CIRRHOSIS. *(E.)* Kehayoglou, K.; Hadziyannis, S.; Kostamis, P.; Malamos, B. (Univ. Athens, Sch. Med., Greece). *Gut* 14(8):653-656, 1973.

Calcium absorption, as measured by whole-body retention of isotopic ^{47}calcium, was investigated in 10 controls and 10 patients (all females, aged 43-62 yr) with primary biliary cirrhosis of 1-5 yr duration before and after medium-chain triglyceride therapy. Absorption of calcium was impaired in 8 patients with primary biliary cirrhosis, 3 of whom had normal serum bilirubin. Mean absorption was significantly less in patients with primary biliary cirrhosis than in controls. Impaired calcium absorption correlated well with increased fecal fat excretion and less well with the intensity of jaundice. Osteoporosis was diagnosed radiologically in 7 patients with primary biliary cirrhosis, and calcium absorption was restored to normal in 7 of 8 patients after medium-chain triglyceride therapy. Decrease of steatorrhea, weight gain, and relief of bone pain have been noted in most patients with primary biliary cirrhosis after therapy. It is concluded that bone disease occurs early in primary biliary cirrhosis and early medium-chain triglyceride therapy in these patients is helpful. Such therapy is also recommended for patients with extrahepatic biliary obstruction and parenchymatous liver disease, both of which are accompanied by steatorrhea and malabsorption of calcium.

7885 HEPATIC HYDROTHORAX. *(Ger.)* Schoen, I. (Munic. Hosp., Berlin-Spandau, Germany). *Dtsch. Med. Wochenschr.* 98(13):669-671, 1973.

On the basis of a laparoscopy and histological examination of a liver biopsy, postnecrotic cirrhosis was diagnosed in a 49-year-old woman who was hospitalized after an episode of acute hepatitis with debilitation, weight loss, and jaundice. Liver function normalized after 2 months of (unspecified) treatment, but an exacerbation of cirrhosis, associated with massive ascites, occurred 1.5 yr later. The patient responded to long-term diuretic therapy, but further exacerbations occurred. A pleural effusion, which caused dyspnea on the slightest exertion, developed on the right side 7 yr after onset of cirrhosis. Because 32 liters of fluid were drained from the pleural cavity in a 2-month period, the patient was suspected of having a pleuroperitoneal fistula. This was confirmed by scintigraphic detection of ^{198}Au in the right pleural cavity after the radioisotope had been injected i.p.; no activity was detected on the left pleural cavity. The presence of diaphragmatic lymphatic anastomoses was ruled out. Several months before the patient died of heart and circulatory failure, injection of indigocarmine dye solution i.p. revealed that ascites fluid was passing through several defects in the right diaphragm. Surgery could not be performed because of the patient's poor general condition. Autopsy showed a small, cirrhotic liver, signs of portal hypertension (eosphageal varices and an enlarged, plethoric spleen) with 200 ml of a clear, yellow fluid in the right pleural cavity. Several regions with pleural and peritoneal openings were present on the right side of the central tendon of the diaphragm. Histological examination demonstrated a congenital diaphragmatic anomaly.

7886 DIFFERENTIAL DIAGNOSIS OF VARIOUS FORMS OF CIRRHOSIS FROM IMMUNOLOGICAL AND MORPHOLOGICAL FINDINGS. *(Ger.)* Vido, I.; Brunner, G.; Selmair, H.; Becker, H. (Med. High Sch., Hannover, Germany). *Dtsch. Med. Wochenschr.* 98(10):472-475, 1973.

Serum immunoglobulin (Ig) fractions were determined quantitatively on 128 patients with cirrhosis. These included 30 with hepatic, 65 with alcohol-toxic, and 33 with primary biliary cirrhosis. In all cases the diagnosis had been confirmed by laparoscopic findings or histological examination of punch liver biopsies and the activity of the disease process determined. Mean values for serum IgG, IgA, and IgM were increased in all 3 types of cirrhosis except for a decrease in mean values of IgA in patients with primary biliary cirrhosis. The increases were statistically significant for IgG in hepatic cirrhosis, for IgA in alcohol-toxic cirrhosis, and for IgM in primary biliary cirrhosis. Significant decreases were found in the ratios for IgG/IgA in alcohol-toxic cirrhosis and for IgG/IgM in primary biliary cirrhosis. In hepatic cases the values for these ratios lay between 7.8 and 12.0 and were not significantly changed. Therefore, it is possible to differentiate between these 3 active forms of cirrhosis on the basis of the serum immunoglobulin values.

7887 FEATURES OF SJOGREN'S SYNDROME IN PRIMARY BILIARY CIRRHOSIS. *(E.)* Alarcon-Segovia, D.; Diaz-Jouanen, E.; Fishbein, E. (Natl. Inst. Nutr., Mexico City). *Ann. Intern. Med.* 79(1):31-36, 1973.

The ocular and salivary components of Sjögren's syndrome were investigated in 14 patients (12 females and 2 males, aged 14 to 60 yr) with primary biliary cirrhosis of 1 to 9 yr duration with a battery of tests that included Schirmer's test; rose bengal staining; parotid secretory sialography; scintillation scanning of salivary glands with ^{99m}Tc pertechnetate; radioactive counts in saliva at 15 and 60 min after i.v. injection of the same radionuclide, as an index of salivary gland function; and histologic study of minor salivary gland specimens obtained by lip biopsy. BSP retention ranged from 13.0 to 33.0% in 30 min; alkaline phosphatase ranged from 10.80 to 34.05 Bodansky U. Abnormalities of lacrimal or salivary glands were detected by 2 or more tests in all patients. The presence or degree of ocular and salivary components of Sjögren's syndrome did not correlate with the duration or the degree of liver disease, the presence of autoantibodies, or the levels of immunoglobulins. These findings indicate that primary biliary cirrhosis is a systemic disease and supports the hypothesis that it is autoimmune in origin.

7888 HEPATORENAL SYNDROME: STUDY OF CLINICAL CHARACTERISTICS IN A LARGE SERIES. *(E.)*

Bern, M. M. (Charity Hosp., New Orleans, La.). *South. Med. J.* 66(7):775-778, 1973.

Hepatorenal syndrome was noted in 31 (12.7%) of 244 patients with cirrhosis of the liver. Of the 31 patients, 22.1% had elevated blood urea nitrogen levels. SGOT ranged from 42-820 U, alkaline phosphatase from 5.6-132 Bodansky U, total bilirubin from 1.4-42.4 mg/100 ml, and BSP retention at 45 min from 10.1-69.4%. These values often overlapped those found in patients with cirrhosis of the liver without hepatorenal syndrome. Neomycin (2-6 gm/day, p.o. for 2-8 days), biliary tree operations, portacaval shunts, and paracentesis did not appear to precipitate hepatorenal syndrome. In patients with the syndrome, gastrointestinal bleeding occurred in 61.3% and ascites in 71% as compared to 23.5% and 36.1%, resp., of cirrhosis patients without hepatoreanl syndrome. Diuretic therapy also appeared more frequently in the case histories of those with hepatorenal syndrome. The prognosis for death while in hepatorenal syndrome did not correlate with ascites or diuresis, but did correlate with gastrointestinal bleeding. Of the small group of patients with the syndrome having portacaval shunts, 100% died. There were 14 deaths caused in order of decreasing frequency by combined hepatic and renal failure, bleeding of the gastrointestinal tract, peritonitis, hepatic failure, cerebral vascular accident, pulmonary embolus, hyperkalemia, and sepsis. Patients in this series who did survive did so with less heroic measures than those who died.

7889 MAXIMAL RATES OF EXCRETION AND SYNTHESIS OF UREA IN NORMAL AND CIRRHOTIC SUBJECTS.

(E.) Rudman, D.; DiFulco, T. J.; Galambos, J. T.; Smith, III, R. B.; Salam, A. A.; Warren, W. D. (Emory Univ. Sch. Med., Atlanta, Ga.). *J. Clin. Invest.* 52(9):2241-2249, 1973.

Normal individuals fed 0.33 g protein N/kg/day excreted 10-15 mg urea N/hr/kg. Ingestion of 0.27 to 1.33 g protein N/kg as casein, ovalbumin, or lactalbumin, accelerated the rate of urea N excretion within 4 hr. A maximum rate of 55 mg urea N/hr/kg was reached with 0.53 g protein N/kg and this persisted for 16 hr. Higher protein doses served only to prolong the duration of maximum excretion. During the 8 hr following doses of 0.53-1.33 g protein N/kg, the blood urea nitrogen level rose by 7-20 mg/100 ml and was stable for 8-28 hr of maximum excretion. Increasing protein above 0.53 g N/kg increased the plasma α-amino N. During infusion of 110 or 165 mg free amino acid N/hr/kg for 12 hr, urea excretion reached the maximum rate produced by 0.53-1.33 g of oral protein. These results indicate that the maximum rate of urinary urea N excretion corresponds to a period of maximal rate of urea synthesis. Oral neomycin reduced the proportion of urea hydrolyzed in the gut to less than 20%. The maximum rate of urinary urea synthesis in 10 normal subjects was 65 mg urea N/hr/kg, compared with 27 mg urea N/hr/kg in 34 cirrhotic patients. It is suggested that measurement of the maximum rate of urinary urea synthesis may lead to earlier detection of cirrhosis, may predict how much dietary protein these patients can tolerate, and may identify patients with greater postoperative risk to encephalopathy.

7890 THE EXOCRINE PANCREAS IN CIRRHOSIS: AUTOPSY AND PANCREATOGRAPHIC STUDY OF 61 CASES. COMPARISON WITH A CONTROL SERIES. *(Fr.)*

Weill-Bousson, M.; Geisler, F.; Weill, J. P. (Univ. Hosp. Ctr., Strasbourg, France). *Arch. Fr. Mal. App. Dig.* 62(1):17-31, 1973.

Histological studies of the liver and pancreas and postmortem pancreatography were performed on 61 patients with cirrhosis (58 with a presumptive diagnosis of alcoholic and 3 with a presumptive diagnosis of posthepatitic cirrhosis) and on 57 age- and sex-matched controls with no clinical evidence of alcoholism, cirrhosis, or polyneuritis. No significant differences were found between the 2 groups. Pancreatic abnormalities were present in 46 (73.8%) of the cirrhotics and in 43 (79.9%) of the controls. Chronic pancreatitis was diagnosed in 2 controls but in none of the cirrhotics. The incidence of pancreatic fibrosis and steatosis was about the same in both groups. Gross or microscopic atherosclerosis was present in 61 (29 of the cirrhotics and 32 of the controls) of the 89 subjects in both groups who had pancreatic abnormalities. This high incidence of atherosclerotic lesions is attributed to the relatively advanced age of patients in both groups. Postmortem pancreatography, performed on 44 cirrhotics and 42 controls, showed that minor anomalies were nonspecific for cirrhosis and were generally associated with pancreatic fibrosis or steatosis. The nonspecific pancreatic abnormalities found in this group of cirrhotics conflict with the conventional view that chronic pancreatitis is frequently associated with cirrhosis.

7891 TREATMENT OF CIRRHOTIC ASCITES BY MECHANICAL INTRAVENOUS REINFUSION (RHODIASCIT SYSTEM). PRELIMINARY RESULTS. *(Fr.)*

van Waes, L.; van Quickenborne, G.; Demeulenaere, L. (St. Andre Clin., Tielt, Belgium). *Acta Gastroenterol. Belg.* 36(3): 200-212, 1973.

Over a 10-month period the Rhodiascit^R system was used 19 times to reinfuse ascites fluid into 9 patients (6 men and 3 women, aged 34-71 yr) with cirrhosis. This system pumps ascites fluid through an ultrafilter which removes substances with molecular weights exceeding 30,000 i.e., proteins and lipids, before reintroducing the fluid i.v. A monitoring system makes it possible to regulate the rate of ltrafiltration and thus the protein concentration f reinjected fluid. Prior treatment had included iet (6 cases), diuretics (6), paracentesis (3), and portacaval shunt which later thrombosed (1). Re-nfusion of ascites fluid was combined with diet 6 cases) spironolactone (5), portacaval shunt urgery (2), and splenorenal shunt surgery (1). scites was controlled in 3 patients, recurred in others, and 3 patients died of gastrointestinal leeding (2 cases) and postoperative liver coma 1 case). Most objective clinical complications ere mild and included fever (14 of 19 procedures), ncreased pulse (13), and increased arterial pressure 17), but one patient developed intravascular clotting.

892 JUVENILE CIRRHOSIS IN SIBLINGS: OBSERVATION ON THE CLINICAL COURSE. *(Ger.)* Berghoff, .; Hohler, H.; Jahnke, K.; Liebegott, G. (Ferdinand auerbruch Munic. Hosp., Wuppertal-Elberfeld, Germany). *ed. Welt* 23(41):1431-1433, 1972.

uvenile cirrhosis was diagnosed in an 18-yr-old male atient and his 11-yr-old sister. Both patients eveloped jaundice at about the same time, and in oth cases the course was complicated by hemolytic nemia with a decrease in the platelet count and actors constituting the prothrombin complex. In both ases laparoscopy showed cirrhosis with small to edium-sized nodules and inflammation. Histological xamination of a biopsy taken from the girl revealed hat the nodules were surrounded by rapidly pro-iferating connective tissue, and periportal infil-rates consisted of lymphocytes; liver cell necrosis as manifested by nuclear pyknosis. The male patient ad a positive test for lupus erythematosis factor. ests for Australia antigen had been negative in both atients until a positive test was obtained in the ister during a recent exacerbation in which hemoglo-in levels did not decrease because of hemolysis. he male patient died 4 yr after onset in a hepatic oma with recurrent bleeding. Autopsy findings sup-ort a diagnosis of posthepatitic cirrhosis resulting rom chronic active hepatitis. His sister has shown ome response to administration of corticosteroids, zathioprin, and prophylactic transfusions of plate-ets and clotting factors.

893 MECHANISMS IN THROMBOCYTOPENIA IN CIRRHOSIS. *(Fr.)* Ardaillou, N.; Yvart, J. (St. Louis osp., Paris, France). *Arch. Fr. Mal. App. Dig.* 2(3):211-216, 1973.

o establish mechanisms involved in thrombocytopenia, latelet lifetime and site of platelet destruction ere determined by injecting ^{51}Cr-labeled platelets nto 39 cirrhotics (37 with alcoholic cirrhosis and each with posthepatic and biliary cirrhosis). All f the patients had thrombocytopenia. No correlation as found between the platelet count and liver function serum albumin concentration and BSP retention) or etween the serum α-globulin concentration and the latelet count. A barely significant inverse rela-ion was found between the serum bilirubin concentration and platelet count ($p < 0.10$). In 16 patients thrombocytopenia was due to pure hypersplenism: the spleen was palpable in all of these patients. This was associated with a low WBC and moderate anemia. In 4 patients thrombocytopenia resulted from a disorder in platelet production; no anemia was present and WBC was only slightly decreased. No evidence of macrocytosis or reticulocytopenia was found. Bone marrow megakaryocytes were normal in 3 and decreased in 1 patient. Increased peripheral platelet destruction was diagnosed in 6 cases. Two mechanisms were implicated in at least 13 of these 39 patients: either increased peripheral platelet destruction and hypersplenism or increased peripheral platelet destruction and disorders in platelet production.

7894 ASYMPTOMATIC PRIMARY BILIARY CIRRHOSIS. *(E.)* Fox, R. A.; Scheuer, P. J.; Sherlock, S. (Roy. Free Hosp., London, England). *Gut* 14(6): 444-447, 1973.

Histological features of stage 1 primary biliary cirrhosis were detected in 4 asymptomatic women, aged 23-54 yr. One was suspected of having rheumatoid arthritis; the second was detected in a family study of hyperparathyroidism; the third, who presented with menorrhagia, had hepatomegaly; and the fourth, who had incapacitating rheumatoid arthritis, was detected during routine antibody screening. The mitochondrial antibody was positive in a titer of 1:128 in 3 subjects and positive in a titer of 1:256 in the 4th. Serum alkaline phosphatase ranged from 22-44 King-Armstrong U/100 ml and serum cholesterol from 200-334 mg/100 ml. All needle biopsies showed pathognomonic bile duct lesions. In all 4 cases there was a surrounding lymphocytic and epithelioid-cell reaction and in 3 actual granulomas were seen. Only the patient with rheumatoid arthritis had impaired lymphocyte transformation in response to phytohemagglutinin. Thus, it seems likely that depression of delayed hypersensitivity responses in primary biliary cirrhosis is a result of the disease and not related to the cause.

7895 PORTAL HYPERTENSION CAUSED BY AN ARTERIOVENOUS ANEURYSM OF THE RIGHT GASTROEPIPLOIC VESSELS AFTER GASTRECTOMY. *(Fr.)* Morand, P.; Potier, N.; Barsotti, J.; Raynaud, R. (Bretonneau Hosp., Tours, France). *Sem. Hop. Paris* 49(25):1837-1843, 1973.

An 82-year-old woman, who had undergone gastrectomy 12 yr previously for a gastric ulcer, was hospitalized with symptoms of portal hypertension (ascites, splenomegaly, varices in the lower 1/3 of the esophagus, and subcutaneous collateral circulation of the portocaval type). A large paraumbilical mass was the site of a continuous loud murmur. Hemodynamic studies confirmed the presence of an arteriovenous shunt, and selective angiogrpahy of the celiac trunk revealed an arterioportal fistula between the right gastroepiploic artery and the superior mesenteric vein. Liver function remained normal, and no histological changes were found when a liver biopsy was examined by light microscopy. Electron microscopy showed enlargement of Disse's spaces with the appearance of collagen fibers and dilatation of biliary canaliculi without pigment deposition. In addition to degenerative changes in the mitochondria, glycogen storage and depletion were observed along with cytolysis and vacuolar necrosis. The mitochondrial changes suggested that reversible changes had occurred in cell respiration as a result of portal hypoxia. After resection of the aneurysm, which was the size of an orange, the patient recovered uneventfully. A biopsy, performed 6 months later, showed that the ultrastructural changes in the liver had disappeared.

7896 BLOOD GASES AND ACID-BASE DISTURBANCES OF ARTERIAL BLOOD IN CHRONIC LIVER DISEASE.

(E.) Kardel, T.; Rasmussen, S. N. (Gentofte Hosp., Copenhagen, Denmark). *Scand. J. Clin. Lab. Invest.* 31(3):307-309, 1973.

Arterial blood pH, P_{CO_2}, standard bicarbonate, P_{O_2}, and oxygen saturation were determined in 32 patients (aged 21-71 yr) with cirrhosis. Patients were fasting, resting in bed, and breathing ambient air. A quantitative parameter of liver function was obtained by measuring the galactose elimination capacity. Studies were performed on 7 patients before and after portacaval shunt surgery. No significant differences were found between blood gas and acid-base findings in patients with good and impaired liver function or in patients with and without portacaval shunt surgery. These results indicate that neither halving of mass function of the liver, nor a maximal portal-systemic shunting of blood, nor the combination of these 2 under basic conditions trigger the hyperventilation and arterial desaturation mechanism which often accompany the clinical syndrome of hepatic coma.

7897 CIRRHOSIS IN AN ADULT WITH EMPHYSEMA AND ALPHA$_1$-ANTITRYPSIN DEFICIENCY.

(E.) Babb, R. R.; Lillington, G. A.; Kempson, R. L. (Palo Alto Med. Clin., Calif.). *Am. J. Dig. Dis.* 18(9):803-807, 1973.

A 68 yr old male farmer, with a history of dyspnea, presented with mid-abdominal pain which he had experienced recurrently for several years. The attacks were usually associated with distention. There was no history of alcohol consumption, blood transfusions, or exposure to farm sprays or potentially hepatotoxic materials, and smoking had been stopped 12 yr earlier. The patient's father died at age 35 yr of unexplained causes. The patient's son, now 28 yr of age, had had "childhood asthma". On admission total bilirubin was 1.7 mg/100 ml; alkaline phosphatase, 130 IU; and SGOT, 81 U. The chest roentgenogram indicated moderately severe hyperaeration of the lungs. On laparotomy the liver was found to be enlarged and grossly cirrhotic. Biopsy indicated micronodular cirrhosis. Regenerative nodules were present and surrounded by dense fibrous bands revealing a lymphatic infiltrate and bile duct proliferation. The patient returned 1 yr later with persistent peripheral edema and ascites. Total bilirubin was 3.0 mg/100 ml; alkaline phosphatase, 195 IU; and SGOT, 75 U. Serum protein electrophoresis revealed an alpha$_1$-globulin concentration of 2%. A test for alpha$_1$-antitrypsin showed a level of 38 mg/100 ml, confirming the diagnosis of alpha$_1$-antitrypsin deficiency.

7898 CHANGES IN IMMUNOGLOBULINS DURING ACUTE AND CHRONIC LIVER DISEASES.

(Ger.) Neumayr, A.; Peschl, L.; Rettenbacher-Daubner, H. (Empress Elisabeth Hosp., Vienna, Austria). *Med. Klin.* 66(50):1728-1733, 1971.

Determinations of IgA, IgM, and IgG were performed by radial immunodiffusion on serum from 17 patients with acute hepatitis and 52 patients with cirrhosis. Because of the severity of their symptoms and bilirubin levels of more than 20 mg/100 ml, prednisolone (25-35 mg/day) was given to 6 patients with acute hepatitis. Histories of consumption of at least 1/2 liter of wine were obtained in 24 of the cirrhotics; 14 of the 52 cirrhotics developed hepatic coma. At the onset of jaundice all 3 immunoglobulins were increased in acute hepatitis, but this increase was significant only for IgM. Increases in immunoglobulins were more pronounced in prednisolone-treated patients than in untreated patients. Over the 60-day observation period IgA levels remained almost constant. IgG levels remained almost constant in untreated patients but began to decrease on day 21 in those given prednisolone. This decrease reached a maximum between days 41 and 60 and was statistically significant. IgM values remained constant until day 20 in the prednisolone-treated group and then decreased, while a tendency to decrease was noted on day 10 in the untreated group. The difference between IgM values in treated and untreated patients was significant from days 11 through 20. No significant differences were found between any of the immunoglobulin fractions in compensated alcoholic and nonalcoholic cirrhosis. However, there was a significant difference between IgA levels in patients with hepatic coma and those with compensated cirrhosis; this difference was even greater in alcoholic cirrhosis. IgM did not consistently increase in these cirrhotics, even in those with hepatic coma. In contrast to IgM, IgG values were increased, but to different extents, in all patients with hepatic coma. The depression of IgG levels produced by prednisolone was further enhanced when prednisolone was combined with azathioprine. These findings indicate that increases in IgA and IgG are characteristic of progressive cirrhosis.

7899 SELECTION OF PATIENTS WITH PORTAL HYPERTENSION FOR SPLENORENAL SHUNT.

(E.) Campbell, D. P.; Anagnostopoulos, C. E.; Glenn, W. W. L. (Yale Univ. Sch. Med., New Haven, Conn.). *Ann. Surg.* 178(1):70-74, 1973.

Portal-systemic shunts were performed in 76 patients for portal hypertension complicated by bleeding esophageal varices. Portacaval anastomoses were performed in 54 and splenectomy and splenorenal anastomoses in 22. The indications for performing a splenorenal shunt were extrahepatic obstruction in 2 children, aged 6 and 7 yr, severe hypersplenism with intrahepatic obstruction in 7 cirrhotic patients, technical problems preventing portacaval anastomosis (such as acute cholecystitis, adhesions from biliary tract surgery, varix of the portal vein, and adhesions from duodenal surgery), combined intra and extrahepatic portal obstruction in 5 cirrhotic patients and portal hypertension without demonstrable obstruction in 2 patients aged 10 and 22 yr. Follow-up data of these patients who had splenorenal shunts performed and those of patients who had portacaval shunts were compared. In terms of operative mortality, post-operative ammonia intoxication, 5-yr survival, and quality of survival, splenorenal shunts were superior to portacaval shunts. Considering further the preservation of intrahepatic bloodflow, the splenorenal shunt is the procedure of choice in the above groups of patients when a suitable splenic vein is available for splenorenal anastomosis. It may be the procedure of choice in most patients requiring portal-systemic shunting.

7900 CIRRHOSIS AND HEPATOMA OCCURRING AT BOSTON CITY HOSPITAL (1917-1968). *(E.)* Purtilo, D. T.; Gottlieb, L. S. (Armed Forces Inst. Pathol., Washington, D.C.). *Cancer* 32(2):458-462, 1973.

Possible changes in the frequency and etiology of cirrhosis and hepatoma during the past 50 years have been examined. This study included 14,000 autopsy records from 1955-68. Cirrhosis was found in 11.5% of these 14,000 and hepatoma in 0.69%. This prevalence is nearly identical to that previously reported for 1917-1954 time period; no changes occurred in age or sex of the patients. There was a 3-fold increase in the number of Negro patients dying of hepatoma as in the earlier period. Hepatoma developed in 5% of the patients with cirrhosis in the 1955-58 series, compared to 3.2% of those in the 1917-54 series. All types of cirrhosis, except that associated with alcohol, declined in frequency. Alcoholic cirrhosis or fatty nutritional cirrhosis accounted for from 31% to 61% of all types of cirrhosis in the 2 series. A detailed study of 98 subjects dying with hepatoma was made. These hepatomas were classified as hepatocellular carcinoma (71), mixed cholangiohepatocellular carcinomas (13), cholangiocarcinomas (12), and anaplastic carcinomas (2). Hepatoma associated with postnecrotic cirrhosis increased 2-3 times in subjects with hemochromatosis. Chronic alcoholism was the probable pathogenetic agent implicated in the production of fatty nutritional cirrhosis, hemochromatosis, and postnecrotic cirrhosis (56 of these 98 patients). An average of 8 yr passed from the onset of the alcoholic cirrhosis to the appearance of hepatoma in 23 alcoholic patients.

7901 RENAL FUNCTION IN CIRRHOSIS: ANATOMICAL AND CLINICAL CORRELATIONS. *(It.)* Cattani, F.; Natangelo, R.; Schmid, C. (St. Charles Borromeo Hosp., Milan, Italy). *Minerva Med.* 63(51):2768-2781, 1972.

Histological changes were studied at autopsy in the kidneys of 50 patients (31 males and 19 females) with cirrhosis; diabetics and patients with primary progressive kidney disease were excluded. Intracapillary proliferation appeared in the glomeruli of 41 patients and extracapillary proliferation, in 20. Other changes included degeneration of the tubular epithelium in 22%, small infiltration of the stroma in 26%, stromal sclerosis in 32%, and arteriolar sclerosis in 34%. Although glomerular and tubular changes occurred with about equal frequency in men and women, stromal changes occurred much more frequently in women. Renal changes appeared with about equal frequency in the various age groups and were more severe in cirrhotics with impaired liver function and in those who had ascites for a long time. Renal changes occurred more frequently in patients with daily urinary outputs of 500 ml or less than in the group as a whole. Proteinuria was associated with a high incidence of intra- and extracapillary proliferation, while leukocyturia was associated with stromal changes. High blood levels of urea (above 0.50%) and ascites were associated with intra- and extracapillary proliferation and stromal changes. Intra- and extracapillary changes and degeneration of the tubular epithelium were more common among patients with decreased prothrombin activity. Increased BSP retention was correlated with glomerular lesions, while almost all patients with ascites for more than 6 months had glomerular lesions and arteriolar sclerosis. Mesangial changes were frequent in patients with collapse lasting for longer than 24 hr, and patients who died of gastrointestinal bleeding had a high incidence of extracapillary proliferation. No relation was found between any renal change and increased plasma creatinine, decreased glomerular filtration, high uric acid levels, hyperbilirubinemia, high blood sodium levels, hypertension, esophageal varices, splenomegaly, diuretic or corticosteroid therapy, and hepatic coma. It is suggested that both hemodynamic and morphological changes intefere with renal function in most cirrhotics.

7902 PHOSPHOCALCIC METABOLISM IN THE HEPATIC CIRRHOSIS. *(Fr.)* Dechavanne, M.; Prost, G.; Lenglet, J. P.; Tolot, F. (Hosp. Jules Courmont, Pierre Benite, France). *Lyon Med.* 229(11):1085-1088, 1973.

7903 CIRRHOSIS, LIVER CANCER, AND ALCOHOL. *(Ger.)* Schneiderbaur, A. (Munic. Hosp., Wien-Lainz, Austria). *Med. Welt* 20(23):751-754, 1972.

7904 CLINICAL, RADIOLOGICAL, AND ENDOSCOPIC CORRELATIONS IN PORTAL HYPERTENSION DUE TO CIRRHOSIS. RESULTS FROM A STUDY OF 64 CASES. *(Sp.)* de las Casas Alonso, P. (Nuestra Senora de la Candelaria Sanit., Santa Cruz de Tenerife, Canary Islands). *Rev. Esp. Enferm. Apar. Dig.* 40(2):139-152, 1973.

7905 TREATMENT OF SEVERE BLEEDING FROM ESOPHAGEAL VARICES. *(Ger.)* Schroder, R.; Vang, J. (Univ. Hosp., Lund, Sweden). *Schweiz. Med. Wochenschr.* 103(31):1081-1086, 1973.

7906 INTERCAPILLARY GLOMERULOSCLEROSIS IN HEPATIC CIRRHOSIS. *(Ger.)* Wehner, H.; Andler, D. (Pathol. Inst., Univ. Tubingen, Germany). *Virchows. Arch. (Pathol. Anat.)* 360(3):265-272, 1973.

7907 TREATMENT OF DIGESTIVE BLEEDING DUE TO EXTRAHEPATIC PORTAL HYPERTENSION BY OESOGASTRIC RESECTION. *(Fr.)* Maillard, J. N.; Bacourt, F. (Fac. Med., Univ. Paris, France). *Arch. Fr. Mal. App. Dig.* 62(5):379-383, 1973.

7908 CLEARANCE AND EXTRACTION OF RADIOACTIVE COLLOIDAL GOLD IN CIRRHOTICS. CHANGES PRODUCED IN THEM BY GELATINE. *(Fr.)* Lebrec, D.; Sicot, C.; Benhamou, J. P. (Beaujon Hosp., Clichy, France). *Biol. Gastroenterol. (Paris)* 6(1):41-48, 1973.

7909 PRIMARY BILIARY CIRRHOSIS IN THE ADULT. *(Fr.)* Coulbois, J.; Dupuy, P.; Bergue, A. (no affil.). *Concours Med.* 95(3):329-337, 1973.

7910 CHANGES IN LEUKOCYTE ALKALINE PHOSPHATASE (LAP) IN ACUTE AND CHRONIC LIVER DISEASE. *(Ger.)* Krug, K.; Stenzel, L. (2nd Med. Clin. Polyclin., Martin Luther Univ., Halle-Wittenberg, Germany). *Folia Haematol. (Leipz.)* 99(2/3):170-179, 1973.

7911 THROMBOCYTIC ENZYMES (LDH, G-6-PDH) IN CHRONIC HEPATITIS AND LIVER CIRRHOSIS. *(Ger.)* Kiss, A.; Sari, B.; Jako, J.; Zayzon, R.; Dan, S. (Med. Univ., Debrecen, Hungary). *Folia Haematol. (Leipz.)* 99(2/3):180-190, 1973.

7912 HEPATOTOXICITY OF LONG-TERM METHOTREXATE THERAPY FOR PSORIASIS. *(E.)* Tobias, H.; Auerbach, R. (New York Univ. Sch. Med., N.Y.). *Arch. Intern. Med.* 132(3):391-396, 1973.

7913 THE SMALL INTESTINE IN LIVER CIRRHOSIS. CLINICAL, LABORATORY, HISTOLOGICAL, IMMUNOLOGICAL AND BACTERIOLOGICAL CHARACTERISTICS. *(Fr.)* Cornet, A.; Hartmann, L.; Courtois, J. E.; Dubrisay, J.; Demelier, J. F.; Barbier, J. P.; Renault, P.; Carnot, F.; Debetz, J.; Dadoune, J. P. (Laennec Hosp., Paris, France). *Sem. Hop. Paris* 49(23):1639-1648, 1973.

7914 SUCCESSFUL TREATMENT OF HEPATIC COMA, COMPLICATED BY RENAL FAILURE, WITH EXCHANGE TRANSFUSION AND PERITONEAL DIALYSIS. *(E.)* York, E. L.; Grieve, S.; Mieny, C. J. (Coronation Hosp., Johannesburg, South Africa). *S. Afr. Med. J.* 47(15):655-656, 1973.

7915 A TECHNIQUE FOR MESENTERICOCAVAL SHUNT. *(E.)* Stipa, S.; Thau, A.; Cavallaro, A.; Rossi, P. (Dept. Surg., Univ. Rome, Italy). *Surg. Gynecol. Obstet.* 137(2):285-287, 1973.

7916 AUTOIMMUNITY IN CIRRHOSIS. (CLINICAL CONTRIBUTION). *(Ger.)* Schneiderbaur, A.; Rettenbacher, F. (Munic. Hosp., Wien-Lainz, Austria). *Wien. Med. Wochenschr.* (suppl. 1):1-26, 1973.

7917 STUDIES OF BLOOD COPPER LEVELS IN CIRRHOSIS. *(Sp.)* Rodriguez Cuartero, A.; Mora Lara, R. J.; Pelaez Redondo, J. (Dept. Internal Med., Univ. Granada, Spain). *Rev. Esp. Enferm. Apar. Dig.* 39(4):411-418, 1973.

7918 INFANTILE CIRRHOSIS WITH HEREDITARY ALPHA$_1$-ANTITRYPSIN DEFICIENCY. CLINICAL IMPROVEMENT IN TWO SIBLINGS. *(E.)* Talamo, R. C.; Feingold, M. (Harvard Med. Sch., Boston, Mass.). *Am. J. Dis. Child.* 125(6):849-847, 1973.

7919 EFFECT OF END-TO-SIDE AND SIDE-TO-SIDE PORTACAVAL SHUNT ON LIVER FUNCTION. *(E.)* Reichle, F. A.; Siplet, H.; Tomasello, P. A.; Alfonso, A.; Reichle, R. M.; Essa, N.; Rosemond, G. P. (Temple Univ. Health Sci. Ctr., Philadelphia, Pa.). *Am. J. Gastroenterol.* 60(2):114-121, 1973.

7920 FUNCTIONAL VENAL CAVAL OBSTRUCTION IN CIRRHOTICS. *(E.)* Lawrence, T.; Myerson, R. M. (VA Hosp., Philadelphia, Pa.). *Am. J. Gastroenterol.* 60(2):135-141, 1973.

7921 URINARY STEROID OUTLINE IN CIRRHOSIS, STUDIED BY GASEOUS PHASE ANALYTICAL METHOD. *(Fr.)* Elkaim, R.; Micoud, M.; Madani, C.; Hadjian, A. J.; Chambaz, E. M. (no affil.). *Ann. Endocrinol. (Paris)* 34(3):241-260, 1973.

7922 JUVENILE CIRRHOSIS AND ALPHA$_1$-ANTITRYPSIN DEFICIENCY. REPORT OF A CASE. *(Fr.)* Gubert, J. P.; Gallet, J. P.; Babinet, J. M.; Saint-Jaques, I. (Herold Hosp., Paris, France). *Ann. Pediatr.* 21(5):463-467, 1973.

7923 DETERMINATION OF RENIN ACTIVITY IN THE PLASMA IN EDEMATOUS LIVER CIRRHOSIS. INFLUENCE

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sp. No. 52, Moscow, USSR). *Arkh. Patol.* 34(10):69-
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Losowsky, M. S.; Scott, B. B. (Univ. Dept.
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, I. C.; Saha, K.; Gupta, S. (Maulana Azad Med.
ll., New Delhi, India). *Indian J. Med. Res.*
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HOSIS: PART I. *(E.)* Singh, H.; Gupta,
L. (Med. Coll., Haryana, India). *Indian J. Med.*
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ANTIGEN IN HEALTHY CARRIERS, LEPROSY, CIRR-
SIS OF THE LIVER AND ACUTE HEPATITIS. *(E.)*
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HOOD CIRRHOSIS. *(E.)* Singh, H.; Dhatt,
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7931 SCINTIGRAPHIC DEMONSTRATION OF ABDOMINAL WALL COLLATERAL VENOUS BLOOD POOL IN CIRRHOSIS. *(E.)* Parkey, R. W.; Bonte, F. J. (Univ. Texas Southwestern Med. Sch., Dallas). *J. Nucl. Med.* 14(2):110-112, 1973.

7932 PECULIARITIES OF HISTAMINE METABOLISM IN CHRONIC HEPATITIS AND LIVER CIRRHOSIS. *(Rus.)* Shastin, N. N. (Leningrad Med. Inst. Sanitation Hyg., USSR). *Klin. Med.* 50(7):39-42, 1972.

7933 THE STATUS OF PORTAL-RENAL ANASTOMOSES IN THE SURGICAL TREATMENT OF PORTAL HYPERTENSION: 21 PERSONAL CASES. *(Fr.)* Saubier, E. C.; Brault, J. A.; Russo, A.; Partensky, C. (Edouard Herriot Hosp., Lyon, France). *Lyon Chir.* 69(4):241-248, 1973.

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7935 PRIMARY BILIARY CIRRHOSIS WITH SCLERODERMA, RAYNAUD'S SYNDROME, TELANGIECTASIA AND THYROID DISEASE. *(Fr.)* Lichtenstein, H.; Poupon, R.; Bodin, F.; Conte Marti, J.; Conte, M. (St. Antoine Hosp., Paris, France). *Sem. Hop. Paris* 49(8):555-559, 1973.

See also, 6547, 6597, 6602, 6609, 6710, 6774, 6800, 6827, 6829, 6859, 6860, 6861, 6890, 7132, 7390, 7132, 7390, 7520, 7538, 7595, 7621, 7625, 7630, 7636, 7675, 7832, 7834, 7841, 7862.

LIVER AND BILIARY TRACT

Gallbladder and Biliary Tract Diseases

36 STUDIES ON HEPATIC BILE ACID SECRETION AND
ITS RELATION TO ADRENAL CORTICOSTEROID
TABOLISM IN PATIENTS WITH CHOLESTASIS. *(Ger.)*
rdes, H.; Kriebel, U.; Littmann, K. P.; Dolle, W. (Med. Clin., Univ. Marburg/Lahn, Germany). *Z. Gastroenterol.* 10(2):78-84, 1972.

To evaluate the effect of disturbances in bile acid excretion on the metabolism of adrenocortical hormones, particularly on the metabolic clearance rate of cortisol, the concentration of bile acids was measured in hepatic bile from 9 patients with obstructive jaundice and in 4 cholecystectomized controls and was correlated with the half-life of cortisol. In obstructive jaundice the mean concentration of total bile acids was 306.3 μg/ml (0.1 mEq/liter). Cholic, chenodeoxycholic, deoxycholic, and lithocholic acids were found in a ratio of 0.6:1.0:0.2:0.1. Apart from traces, no free bile acids or abnormal metabolites were detected. Bile acid concentrations in obstructive jaundice were only 1/10 of control values, and the ratio of cholic acid to chenodeoxycholic acid had decreased from 1.4 in controls to 0.6 in obstructive jaundice. There was a significant correlation between the cortisol half-life and the ratio of chenodeoxycholic to cholic acid. These findings indicate that impaired hepatic extraction of cortisol in obstructive jaundice is caused by: (1) a decrease in bile acids excreted and stored within the cells and (2) impairment of 12-α-hydroxylation of bile acids with a relative increase in the chenodeoxycholic acid concentration. In contrast to patients with cirrhosis, those with objective jaundice excrete normal quantities of cortisol metabolites in their urine. It is concluded that impaired cortisol clearance in liver disease is due, at least partially, to impairment of transport to intracellular sites of metabolism.

7937 ACUTE CHOLECYSTITIS: THE QUESTION OF EARLY OR LATE OPERATION.

(E.) Pheils, M. T.; Andersen, P. T.; Silverton, R. P.; Duraiappah, B. (Repatriation Gen. Hosp., Concord, Australia). *Aust. N.Z. J. Surg.* 43(1):24-27, 1973.

During a 5-yr period 327 elective cholecystectomies were performed on 209 males and 118 females, and 128 cholecystectomies were carried out during an attack of acute cholecystitis on 93 males and 35 females. Patients in the group undergoing surgery during acute cholecystitis were significantly older than those in the elective group. Operative mortality was 1.2% in the elective and 1.6% in the acute groups. In the acute groups 22 had gangrenous gallbladders and 7 had generalized biliary peritonitis. Temporary biliary fistulas (3) occurred exclusively in the acute group and gross infection was also more frequent. Abdominal wound dehiscence was more frequent in the acute group, probably due to the higher incidence of gross wound infection. The acute group had no greater risk of recurrent calculi and no strictures developed in either group. These results support the view of early surgery in cases of acute cholecystitis. In this series 13 cholecystostomies were performed because removal of the gallbladder was either hazardous or technically difficult. This operation did not increase either mortality or serious morbidity. Early operation is urged for older patients, as this group has a higher tendency to gangrene of the gallbladder, responds badly to conservative treatment, and has a higher recurrence rate.

7938 EFFECTS OF PHENOBARBITAL ON BILE SALT METABOLISM IN CHOLESTASIS DUE TO INTRAHEPATIC BILE DUCT HYPOPLASIA.

(E.) Stiehl, A.; Thaler, M. M.; Admirand, W. H. (Dept. Med., Univ. California, San Francisco). *Pediatrics* 51(6): 992-997, 1973.

The effects of phenobarbital on bile salt metabolism in a 4-yr old female with severe cholestasis due to congenital paucity of perilobular bile dusts were studied with ^{14}C-cholate and ^{3}H-chenodeoxycholate. Before phenobarbital was administered cholate was the predominant bile salt in the peripheral blood, whereas chenodeoxycholate was predominant in the total bile salt pool. This difference in distribution was apparently caused by relatively greater impairment of excretion of cholate from the liver cell into the bile. Phenobarbital decreased the total serum bile salt concentration (from 132 to 62 μg/ml), the total bile salt pool (from 412 to 304 mg) and the biologic half-life (cholate from 106 to 34 hr; chenodeoxycholate from 77 to 42 hr). The proportion of the total bile salt pool present in the peripheral blood decreased from 16.8% to 11.7%. Phenobarbital markedly increased the fecal bile salt excretion. These data suggest that phenobarbital improves pruritus in tyis type of intrahepatic cholestasis by reducing serum bile salt concentrations. This is accomplished by a shift in bile salts from the peripheral blood into the enterohepatic circulation and by enhancing fecal bile salt excretion.

7939 SENSITIVE BIOASSAY OF CHOLECYSTOKININ IN HUMAN SERUM.

(E.) Johnson, A. G.; McDermott, S. J. (Charing Cross Hosp. Med. Sch., London, England). *Lancet* (7829):589-591, 1973.

A bioassay of cholecystokinin in human serum was designed. It is a modification of a superfusion technique using isolated rabbit gallbladder strips. Fasting and postprandial levels were measured in 20 healthy individuals (10 male and 10 female). The mean fasting level was 92 m Ivy dog units/ml and was similar in males and females. These are comparable to results obtained in a preliminary report with radioimmunoassay. The mean level in males 20 min following a meal was 195 m Ivy dog units/ml and was significantly higher than females, 134 m Ivy dog units/ml. In 5 patients following Polya gastrectomy, both the fasting and postprandial levels were significantly lower than in healthy controls. The test seems specific (except for cerulein), sensitive, reproducible, and practical.

7940 LIVER FUNCTION IN PATIENTS WITH CHOLEDOCHODUODENOSTOMY AFTER BENIGN BILIARY DISEASES.

(Ger.) Keclik, M.; Huslarova, A.; Hyanek, J. (Med. Fac., Charles Univ., Prague, Czechoslovakia).

Z. *Gastroenterol.* 10(5):333-338, 1972.

To determine whether choledochoduodenostomy causes liver damage by producing progressive cholangitis, long-term follow-ups were made on 48 patients (34 women and 14 men, aged 27-75 yr) who underwent this procedure for choledocholithiasis or stenosis of the papilla of Vater or biliary tract with dilatation of the common bile duct. Patients whose anastomoses were not visualized by barium contrast were not included in this study since their anastomoses might be stenotic. Controls consisted of 26 cholecystectomized patients who had no postoperative signs of inflammation or obstruction. Among the patients who had undergone choledochoduodenostomy, significant improvements occurred in values for serum alkaline phosphatase, SGPT, α- and γ-globulins, and the albumin:globulin ratio. Comparison of these values with those obtained from cholecystectomized controls showed that serum alkaline phosphatase and SGPT values were significantly lower in controls than in patients who had undergone choledochoduodenostomy. No appreciable differences were found in the erythrocyte sedimentation rate or serum albumin or globulin fractions. It is suggested that the greater scattering of SGPT and serum alkaline phosphatase values found in patients who had undergone choledochoduodenostomy are due to changes in the penetrability of the anastomosis which could be caused by mucus, spasms, or partially digested food.

7941 EFFICACY AND SPECIFICITY OF CHENODEOXYCHOLIC ACID THERAPY FOR DISSOLVING GALLSTONES. *(E.)* Thistle, J. L.; Hofmann, A. F. (Mayo Clin., Rochester, Minn.). *N. Engl. J. Med.* 289(13):655-659, 1973.

n a controlled trial, 53 patients (30 males and 23 females) with asymptomatic radiolucent gallstones in functioning gallbladders were treated with chenoeoxycholic acid, (10-26 mg/kg/day) cholic acid, (6-33 mg/kg/day) or placebo. At 6 months, 11 of 18 patients receiving chenodeoxycholic acid had a decrease n gallstone size or number, but no response was oberved in the 17 treated with cholic acid or in the 18 eceiving placebo. Of 7 others on chenodeoxycholic cid for 2-3 yr, 3 had no gallstones, and 3 had continuing reduction in gallstone size. Of 13 patients with radiopaque gallstones, only 2 responded to chenodeoxycholic acid. About one quarter of those ingestng chenodeoxycholic acid had transiently elevated erum glutamic oxalacetic transaminase, but no other liver function abnormalities. Liver biopsies from patients were normal; 3 patients had minor changes. Chenodeoxycholic acid continues to offer a specific medical treatment for asymptomatic radiolucent gallstones in functioning gallbladders.

7942 PRIMARY HEPATIC SYNTHESIS OF MONOHYDROXY BILE ACIDS IN EXTRAHEPATIC BILIARY ATRESIA. *(Ger.)* Back, P. (Med. Clin., Univ. Freiburg/Breisgau, Germany). *Klin. Wochenschr.* 51(18):926-932, 1973.

Among the bile acids found in urine from a 5-month-old boy with extrahepatic biliary atresia were the sulfated esters of conjugated lithocholic (3α-hydroxy-5β-cholanic) and 3β-hydroxychol-5-enoic acids. No bile acids were detected in the feces, while only cholic acid (74.8 μg/ml) and chenodeoxycholic acid (99.5 μg/ml) could be identified in the serum. *In vitro* studies showed that the microsomal fraction of liver homogenate from this patient converted [4-^{14}C]-cholesterol into what has tentatively been identified as 3β-hydroxycholest-5-enoic acid. Liver homogenate, the mitochondrial fraction, and the microsomal supernatant obtained at 9000 x g converted unlabeled 3β-hydroxychol-5-enoic acid to lithocholic and allolithocholic (3α-hydroxy-5α-cholanic) acids. Microsomes + soluble enzymes produced about 4 times as much allolithocholic as lithocholic acid, while mitochondria + soluble enzymes yielded about equal amounts of both bile acids. These findings suggest that conversion of cholesterol to lithotholic acid occurs only if microsomal enzyme systems are absent or severly damaged and mitochondrial and soluble enzymes take part in cholesterol catabolism. Lithocholic acid has been shown to produce portal cirrhosis in rabbits and iguanas.

7943 BILIARY LIPID COMPOSITION IN NORMOLIPIDEMIC AND PREBETA HYPERLIPOPROTEINEMIC GALLSTONE PATIENTS. INFLUENCE OF SUCROSE FEEDING OF THE PATIENTS ON THE BILIARY LIPID COMPOSITION. *(E.)* Cahlin, E.; Jonsson, J.; Nilsson, S.; Schersten, T. (Dept. Surg., Univ. Goteborg, Sweden). *Scand. J. Gastroenterol.* 8(5):449-456, 1973.

Hepatic bile lipid composition was analyzed in 51 patients (16 males and 35 females) with (43) and without (8, peptic ulcer patients) gallstone disease. Gallstone patients had significantly lower concentrations of bile acids and lecithins in hepatic bile, but the cholesterol concentration was the same as in gallstone-free patients. In gallstone patients with pre-beta hyperlipoproteinemia, the concentration of chenodeoxycholic acid was very low, and the concentration of total bile acids and lecithins was significantly decreased as compared with both gallstone-free patients and normolipidemic gallstone patients. Gallstone patients with functioning gallbladder had higher biliary cholesterol concentration than gallstone patients with nonfunctioning gallbladder. Feeding of sucrose for 14 days prior to bile collection did not significantly alter lipid composition in gallstone patinets. It is concluded that the number and rate of enterohepatic circulation of bile acids are important for the lithogenic potential of hepatic bile. It is suggested that comparatively high prevalence of gallstone disease in patients with pre-beta-hyperlipoproteinemia depend on a lipid metabolic defect in the liver.

7944 DISAPPEARANCE AND PROLONGED ABSENCE OF JAUNDICE AND HYPERBILIRUBINEMIA IN CARCINOMA OF THE AMPULLA OF VATER. *(E.)* Oliai, A.; Koff, R. S. (Boston VA Hosp., Mass.). *Am. J. Gastroenterol.* 59(6):518-521, 1973.

A 75 yr old man presented with obstructive jaundice, an enlarged gallbladder, and occult intestinal bleeding. Jaundice and the palpable gallbladder spontaneously disappeared, and serum bilirubin levels remained normal during the final hospital admission 5 months later. Alkaline phosphatase was 49 Bodansky U; SGOT, 180 and SGPT, 73 Karmen U. His history revealed a hemigastrectomy, vagotomy and Billroth II anastomosis performed 8 yr earlier for recurrent upper gastrointestinal bleeding due to peptic ulcer disease. A papillary adenocarcinoma of the ampulla of Vater with metastases to the liver, bones, and adrenals was found. The sequence of obstructive jaundice followed by the prolonged absence of hyperbilirubinemia accompanied by progression of metastases is unusual in papillary carcinoma of the ampulla, and reflects the extraordinary variability in the natural history of untreated ampullary carcinoma.

7945 GAS CHROMATOGRAPHIC STUDIES OF SERUM BILE ACIDS: TECHNIQUE AND RESULTS FROM PATIENTS WITH ACUTE HEPATITIS. *(Ger.)* Erb, W.; Schreiber, J.; Walczak, M. (Ctr. Internal Med., Johann Wolfgang Goethe Univ., Frankfurt/Main, Germany). *Z. Gastroenterol.* 10(5):349-358, 1972.

Bile acid concentrations were determined on serum from (1) 10 patients with acute viral hepatitis 1-3 days after onset of jaundice; (2) 8 patients 10 days after onset of jaundice; and (3) 14 patients after bilirubin was no longer excreted in the urine; 16 patients with no evidence of liver disease served as controls. The patients with hepatitis, aged 18-65 yr, were being fed a high-protein diet containing 56-70 g/day of fat. In group (1) significant increases had occurred in total bile acids and cholic, chenodeoxycholic, and lithocholic acids. Cholic acid, which made up 49.5% of the total in comparison with 9.7% in the controls, was relatively increased, while deoxycholic and lithocholic acids had undergone relative decreases. In group (2) total bile acid levels were still increased, but not to as great an extent as in group (1). Chenodeoxycholic acid constituted an average of 43.5% and cholic acid, 33.7% of the total bile acids. Significances could not be calculated. Lithocholic acid was significantly increased, while deoxycholic acid was significantly decreased. In group (3) total bile acid levels were still increased, but not to as great an extent as in groups (1) and (2). Some findings were in the normal range, while others were still very pathological. The relative increase in cholic acid was still significant. Bile acid values showed a tendency to normalization in sera from 8 patients who had previously been tested. From these findings it is concluded that decreases in secondary bile acids are due to a decrease in bile secretion by the liver, which results in less primary bile acids for the intestinal bacteria to convert into secondary bile acids.

7946 BILE ACIDS IN THE HEPATIC PARENCHYMA IN SUBJECTS WITH CHOLELITHIASIS AND NORMAL SUBJECTS. *(Ger.)* Bruhl, W.; Zepke, D. (Med. Acad., Lubeck, Germany). *Schweiz. Med. Wochenschr.* 103(24):870-873, 1973.

In a postmortem study bile acid concentrations were determined in extracts made from homogenates of the livers of 13 subjects with gallstones (5 male and 8 female) and 10 subjects (5 male and 5 female) without gallstones. The deaths of these subjects, who ranged in age from 65 to 78 yr, could not be attributed to hepatobiliary disease. The concentrations of cholic, chenodeoxycholic, and deoxycholic acids and the ratio of trihydroxy- to dihydroxycholanic acids were significantly decreased in subjects with gallstones. In cholelithiasis changes in hepatic bile acids appear to be more pronounced than those in gallbladder bile acids reported in the literature. It is suggested that the primary disturbance in bile acid metabolism occurs in the liver in cholelithiasis and that liver bile acids are less subject to the effects of the descending biliary tract and enterohepatic circulation, which can both promote and prevent stone formation.

7947 AGE AS A RISK IN CHOLELITHIASIS. *(Ger.)* Grozinger, K. H.; Schar, I. (Munic. Hosp., Leverkusen, Germany). *Med. Welt* 23(1):25-27, 1972.

To determine the effect of age on survival and postoperative complications, a comparison was made between 604 patients, aged 60 yr or more, and 606 patients, aged 30-39 yr, who were operated on for cholelithiasis. There were more men (30%) among the older patients than among the younger ones (18%). While uncomplicated cholelithiasis was most common among younger patients (409 cases), most of the older patients had cholelithiasis associated with cholecystitis, hydrops, empyema, or gallbladder perforation (199 cases) or cholelithiasis associated with lesions of the extrahepatic biliary tract (207 cases). Only 56 of the younger patients, but 141 of the older patients had histories of biliary tract disease dating back more than 10 yr. Nonfatal postoperative complications occurred in 79 (13%) of the younger patients and 133 (22%) of the older patients; these complications were twice as frequent in older as in younger men. Only 5 (0.8%) of the younger patients died postoperatively compared to 69 (11.3%) of the older group. The higher incidence of complications and deaths in elderly patients is due not only to diseases associated with aging, but can also be attributed to atypical symptoms, poor preparation for surgery, and particularly the postponement of surgery in complicated cholelithiasis. If elderly patients do not respond promptly to conservative therapy, surgery should be performed without delay.

7948 CHOLESTATIC SYNDROMES IN INFANCY: DIAGNOSTIC VALUE OF SERUM BILE ACID PATTERN AND CHOLESTYRAMINE ADMINISTRATION. *(E.)* Javitt, N. B.; Morrissey, K. P.; Siegel, E.; Goldberg, H.; Gartner, L. M.; Hollander, M.; Kok, E. (Cornell Univ. Med. Coll. New York, Hosp., N.Y.). *Pediatr. Res.* 7(3):119-125, 1973.

A group of 7 children with biliary atresia and other cholestatic syndromes were followed for as long as 2 years. Of the 7, 5 entered the program at birth and 2 entered at 2 yr of age. Serum bile acid levels were determined periodically before, during, and after treatment with cholestyramine (4-12 g/24 hr). The initial serum bile acid pattern in 4 infants with extrahepatic biliary atresia showed predominantly chenodeoxycholic acid. Cholestyramine administration had relatively little effect on the total serum bile acid level and caused only a slight increase in the cholate to chenodeoxycholate ratio (e.g., from less than 1 to a maximum of 1.3). Three infants with intrahepatic cholestatic syndromes had predominantly cholic acid in plasma and cholestyramine administration caused a reduction in the total serum bile acids with a marked increase in the cholate to chenodeoxycholate ratio (e.g., from 3.5 to 13). The initial serum bile acid patterns and response to cholestyramine appear to distinguish between extrahepatic biliary atresia and other cholestatic syndromes. No problems with bowel motility arose during this study as a result of cholestyramine.

7949 EFFECT OF PHENOBARBITAL ON HYPERLIPEMIA IN PATIENTS WITH INTRAHEPATIC AND EXTRAHEPATIC CHOLESTASIS. *(E.)* Linarelli, L. G.; Hengstenberg, F. H.; Drash, A. L. (Mercy Hosp., Pittsburgh, Pa.). *J. Pediatr.* 83(2):291-298, 1973.

Paucity of intrahepatic bile ducts in 4 children (aged 3-11 yr) and complete extrahepatic biliary atresia in another child (2 months old) were treated with phenobarbital (final dose 6 to 12 mg/kg/day). No adverse effects were noted during phenobarbital therapy. Clinical improvement, manifested by some relief of pruritus and decreased size and number of xanthomata, occurred. An average of 50% reduction in free cholesterol and triglycerides. Serum bilirubin, transaminase, and alkaline phosphatase values were not significantly changed. There were significant improvements in lipoprotein electrophoretic patterns. The mechanism of the hypolipemic effect of phenobarbital was unclear. Phenobarbital is known to reduce the concentration of serum bile salts and to increase the hepatic excretion of the bile salts. The latter mechanism may be a partial explanation for some of the hypolipemic effects, especially in patients with paucity of intrahepatic bile ducts. These data suggest that phenobarbital is helpful in the management of hyperlipemia as well as of hyperbileacidemia and hyperbilirubinemia in cholestatic conditions.

7950 FAT ABSORPTION IN CONGENITAL OBSTRUCTIVE LIVER DISEASE. *(E.)* Glasgow, J. F. T.; Hamilton, J. R.; Sass-Kortsak, A. (Dept. Pediatr., Univ. Toronto, Canada). *Arch. Dis. Child.* 48(8): 601-607, 1973.

A study was made of 15 children (4 males and 11 females; 2-93 months) with congenital obstructive liver disease. Diagnoses included extrahepatic biliary atresia (8), α_1-antitrypsin deficiency (1), benign recurrent cholestasis (1), and idiopathic obstructive jaundice (5). Fecal fat excretion exceeded 15% of the dietary intake in all but 4 cases. Lecithin administered (p.o. as part of the diet, 1g lecithin to 5g dietary fat) to 7 patients failed to improve fat absorption. Proximal intestinal contents sampled during digestion of a standard fat-containing meal showed impaired solubilization of lipid in the aqueous phase, which reflected the severity of the steatorrhea. There was a close positive correlation between the degree of fat solubilization and the luminal concentration of bile salts. A proportion of dietary fat was solubilized and absorbed even in the absence of detectable bile salts. This study demonstrates the importance both of bile salts in normal assimilation of fat and of alternative absorption pathways in biliary obstruction.

7951 EXTRAHEPATIC BILIARY ATRESIA: DIAGNOSIS BY SERUM BILE ACID PATTERNS AND RESPONSE TO CHOLESTYRAMINE. *(E.)* Morrissey, K. P.; Javitt, N. B. (Cornell Univ. Med. Coll., New York, N.Y.). *Surgery* 74(1):116-121, 1973.

By gas liquid chromatographic analysis of serum bile acid patterns before and after a trial of cholestyramine therapy 5 children (2 females and 3 males, aged 10 months-15 days) with extrahepatic biliary atresia were distinguished from 4 children (2 females and 2 males aged 5 days-7½ yr) with cholestatic syndromes and patent bile ducts. All children had similar clinical syndromes of jaundice in the neonatal period. Of the 9 children, 8 underwent laparotomy between 2 and 6 months of age. In the group with atresia, chenodeoxycholate was the predominant bile acid in serum, and the group average cholate/chenodeoxycholate ratio of 0.3 did not increase above 1.0 during a trial of cholestyramine. In the group with patent bile ducts cholate was the predominant bile acid in serum, and the group average cholate/chenodeoxycholate ratio of 3.1 increased to 5.3 after 2½ to 7 weeks of cholestyramine. Long-term therapy in 3 children with patent bile ducts resulted in a further increase in the ratio and significant reduction in total serum bile acid levels. Failure of response to cholestyramine is consistent with a completely interrupted enterohepatic circulation and appears to be a relatively rapid, noninvasive method for differentiating complete obstruction of the bile ducts from cholestatic conditions that do not require operation.

7952 INTRAHEPATIC BILIARY ATRESIA. *(Sp.)* Ruiz, A.; Valbuena, L.; Picazo, L. (La Paz Munic. Sanit., Madrid, Spain). *Rev. Esp. Enferm. Apar. Dig.* 39(2):143-170, 1973.

Clinical and autopsy findings are described for 14 infants (10 boys and 4 girls) with intrahepatic biliary atresia. The onset of symptoms ranged from birth in 3 cases to 45 days in all but 1 infant who developed manifest jaundice at 3 months. Patients were moderately to severely underdeveloped. Abnormalities in clotting were manifested by purpura and umbilical bleeding, and prothrombin was significantly decreased but responded to vitamin K therapy. The extrabiliary tract was radiologically normal, but contrast medium failed to pass into the liver. Increases were noted in bilirubin, particularly direct bilirubin; serum alkaline phosphatase activities; and cholesterol levels. SGOT and SGPT activities were slightly increased, but flocculation tests for liver function remained normal or were slightly abnormal. Associated diseases included cardiac malformations in 3 cases; harelip with a velopalatine fistula and bone changes in a girl with an abnormal karyotype and cytomegalic inclusion disease; and esophageal atresia with a tracheoesophageal fistula. Autopsies, performed on 9 patients, showed that none had died of liver failure but of infectious disease (bronchopneumonia, giant cell pneumonitis, encephalitis), respiratory involvement (atelectasia, pulmonary bleeding), and a girl with generalized gangliosidosis developed candidiasis. The most marked changes found in liver biopsies were inflammation and changes in hepatocytes which resulted from cholestasis. Vascular changes and fibrosis, which was not related to age, were minimal.

7953 CHOLECYSTOLITHOTOMY: A FOLLOW-UP INVESTIGATION.

(Dan.) Kristensen, H.; Mosegaard, A.; Tarp, M. (Central Hosp., Hjorring, Denmark). *Ugeskr. Laeger.* 134(35):1845-1846, 1972.

Of 110 patients who had undergone cholecystolithotomy 1-11 yr earlier (average of 7.1 yr), 97 answered questionnaires and 80 underwent oral cholecystography; 7 patients could not be traced and 6 had died. Of those who died, 3 died of gastrointestinal cancer, 2 of cardiovascular disease, and 1 of biliary tract cancer; at autopsy a solitary stone was found in the gallbladder of the last patient. The 97 patients (85 women and 12 men) were divided into 4 groups: (1) 40 were asymptomatic and had good gallbladder function with no evidence of gallstones; (2) 15 had dyspepsia or episodes of pain similar to that before surgery but had normally functioning gallbladders and no recurrence of stones; (3) 25 patients had radiologically confirmed gallstones and another 3 had undergone cholecystectomy for recurrent stones; and (4) 14 patients were unable to undergo cholecystography but did answer the questionnaire. Of the 25 patients with recurrent stones, 15 were asymptomatic. While 84 patients were satisfied with the results of surgery, 15 had episodes of pain after the operation and 5 were dissatisfied with the results of surgery; all 15 had normally functioning gallbladders. Because of the high incidence of recurrent gallstones, cholecystolithotomy should be reserved for patients whose condition necessitates a limited operation.

7954 THE BACTERIOLOGY OF THE OBSTRUCTED BILIARY TREE.

(E.) Maddocks, A. C.; Hilson, G. R.; Taylor, R. (St. George's Hosp., London, England). *Ann. R. Coll. Surg.* 52(5):316-319, 1973.

Of 142 bile specimens taken at operation from 100 patients with chronic disease of the biliary tree, 114 were infected with bacteria and 28 were sterile. Many specimens yielded more than 1 organisms, giving a total of 191. *Escherichia coli* was isolated with the greatest frequency (75/191) followed by *Klebsiella* (44), *Proteus* (24), and *Pseudomona* (11). Of the 15 antibiotics tested against various bacterial isolates, the most active were erythromycin (100%), gentamicin (91.6%), colistin (85.6%), chloramphenicol (85.5%), and kanamycin (82.6%). Among the antibiotics tested against *E. coli.* and *Klebsiella* separately, gentamicin, colistin, and kanamycin ranked highest in activity. In both cases, gentamicin was 100% effective. These results should be useful in the choice of initial postoperative antibiotics. Once the results of cultures on the patients' own bile are available the antibiotics must be reviewed and altered if necessary.

7955 PREOPERATIVE ANTIBIOTICS IN BILIARY SURGERY.

(E.) Chetlin, S. H.; Elliott, D. W. (VA Hosp., Pittsburgh, Pa.). *Arch. Surg.* 107(2):319-323, 1973.

Prophylactic administration of cephaloridine at midnight (1 g, i.m. before surgery, with preoperative medication, and 6 and 12 hr postoperatively) was evaluated prospectively for its effect on bile cultures and postoperative septic complications in 84 patients undergoing biliary operations. These 84 patients were selected as "high risk" for postoperative sepsis because they were over 70 yr old (34) or had acute cholecystitis (24), obstructive jaundice (19), or common duct stones without jaundice (7). Such patients have previously been shown to have positive bile cultures at operation in 58% to 72% of cases. Cephaloridine failed to reduce the incidence of positive bile cultures; the percentage of positive cultures was 53% for treated and 52% for untreated patients. However, invasive infections occurred in only 4% of 47 treated patients, as compared to 27% of similar, but untreated, controls.

7956 BACTERIOLOGY IN BILIARY TRACT DISEASE AND ITS CORRELATION WITH CHOLELITHIASIS.

(Sp.) Herrera Llerandi, R.; Luna Azurdia, R.; de Villanueva, S. (Herrera-Llerandi Hosp., Guatemala City). *Rev. Col. Med.* 23(1):1-5, 1972.

Cultures were made of bile samples from 267 of 300 patients, mostly Amerindians, who underwent cholecystectomy or choledochostomy for cholelithiasis. The incidence of biliary infections was the same for acute and chronic cholecystitis. Cultures were positive in 100 (37%) and sterile in 167 (63%). The most commonly isolated organisms were coliform bacteria, found in 85 of the 100 infected bile samples. Other bile samples contained *Staphylococcus* (3), *Pseudomonas aeruginosa* (6), *Salmonella* (3), and *Proteus* (3): *Aerobacter aerogenes*, *Bacteroides*, and *Alcaligenes fecalis* were identified in 1 case each. Mixed gallstones, found in 72% of these patients, were accompanied by infection in 36%; bilirubin stones, present in 19%, were associated with in-ection in 25%; and cholesterol gallstones, present n 9%, were accompanied by infection in only 1 ase. Only 2 of the 300 operated patients died, nd both deaths were secondary to shock caused by ram-negative bacteria although broad-spectrum ntibiotics had been administered. One patient had erforated his gallbladder 3 days before hospitaliation and the other had an enterobiliary fistula.

957 SERUM LIPIDS IN CHOLELITHIASIS: EFFECT OF CHENODEOXYCHOLIC ACID THERAPY. *(E.)* ell, G. D.; Lewis, B.; Petrie, A.; Dowling, R. H. Hammersmith Hosp., London, England). *Br. Med. J.* (5879):520-523, 1973.

asting serum lipids were measured in 36 patients 28 females and 8 males; aged 24-75 yr) with preumed cholesterol gallstones. Measurements were aken at monthly intervals for 6 months in 21 of hese 36 patients in whom chenodeoxycholic acid).5-1.5 g/day, p.o.) therapy was started. Before reatment half of the patients had serum cholesterol evels exceeding 260 mg/100 ml or serum triglycerde values greater than 160 mg/100 ml or both. hese lipid levels were significantly greater than hose in control subjects matched for age and sex. reatment with chenodeoxycholic acid did not change erum cholesterol levels but did significantly reuce serum triglyceride concentrations from a prereatment level of 118 mg/100 ml to 95 mg/100 ml fter 6 months of therapy. The mechanism of this riglyceride-lowering action of chenodeoxycholic cid is not known, but it may have therapeutic alue in patients with hypertriglyceridemia.

958 ICTERIC THORACIC DUCT LYMPH: SIGNIFICANCE IN PATIENTS WITH MANIFESTATIONS OF OBSTRUCVE JAUNDICE. *(E.)* Dumont, A. E. (New York Univ. h. Med., N.Y.). *Ann. Surg.* 178(1):53-58, 1973.

evels of bilirubin and protein were measured in horacic duct lymph and in serum in 16 adult patients th clinical manifestations of obstructive jaundice. agnoses in these 16 patients included recurrent holestasis (1), liver disease (3), thorazine jaunce (1), extrahepatic obstruction (8), and cholesasis (3). In contrast to the similarity of the linical picture, several strikingly different paterns in the relation between lymph/serum bilirubin d protein ratios were identified. Assuming that lirubin circulates in body fluids in a protein ound form, the results suggest that in 9 patients cess bilirubin filtered continuously from blood lymph across capillary walls in the liver and trahepatic portal bed. In 5 others additional lirubin entered hepatic lymph from either hepaocytes or leaky canaliculi. In the remaining 2 tients significant amounts of recirculating biliubin were apparently cleared from hepatic lymph as liary secretory function returned. Levels of rculating bilirubin decreased in 11 of 14 patients ollowing diversion of thoracic duct lump from blood, ndicating that a significant component and perhaps 1/2 of the excess circulating bilirubin pool normally entered blood *via* the thoracic duct each 24 hr. As the degree of hyperbilirubinemia bore no relation to lymph/serum bilirubin ratios, explanations of jaundice which relate diffusion into tissue to degree of hyperbilirubinemia are incorrect. Cessation of pruritus following diversion of lymph noted in 4 patients suggests that excess bile salts also recirculate to the blood via lymph.

7959 ALTERED BILE ACID METABOLISM DURING TREATMENT WITH PHENOBARBITONE. *(E.)* Miller, N. E.; Nestel, P. J. (Dept. Clin. Sci., Australian Natl. Univ., Canberra). *Clin. Sci. Mol. Med.* 45(2): 257-262, 1973.

The effects of phenobarbital (60 mg, 4 times/day, 13-18 days) on cholesterol and bile acid metabolism were examined in 4 healthy humans (all male, aged 17-23). In 3 of the 4, the fecal excretion of bile acids was increased by phenobarbital. This was associated with an increased pool size and turnover of cholic acid. Cholesterol excretion was not clearly affected. The fourth subject, who did not respond, was also exceptional in not showing an increase in the plasma clearance of antipyrine. The 3 responsive subjects also developed an average increase of 29 mg/100 ml in plasma cholesterol concentration and an average increase of 25 mg/100 ml in triglyceride concentration. These findings were associated with an early rise in very-low-density lipoprotein and a fall in plasma cholesterol specific radioactivity in 1 patient, changes compatible with increased cholesterol synthesis. It is suggested that the increased bile acid production with phenobarbital may reflect both primary stimulation of cholesterogenesis, as well as induction of enzymes of cholesterol catabolism.

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8007 PRIMARY SEPTIC CHOLECYSTITIS DUE TO CLOSTRIDIUM PERFRINGENS. A CASE REPORT. *(Ger.)* Orth, H. (Munic. Hosp., Frankfurt/Main-Hochst, Germany). *Munch. Med. Wochenschr.* 115(20):916-918, 1973.

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8009 COMPOSITION OF NORMAL AND PATHOLOGICAL HUMAN BILE AND ITS RELATION TO THE CHEMICAL COMPOSITION OF GALLSTONES. *(Sp.)* Arianoff, A. A. (St. Elisabeth Hosp., Louvain, Belgium). *Rev. Esp. Enferm. Apar. Dig.* 39(1):37-42, 1973.

8010 PURIFIED PANCREATIC ENZYMES IN THE GENESIS OF INFLAMMATORY PROCESSES IN THE GALLBLADDER: EXPERIMENTAL STUDY. *(Sp.)* Gramatica, L. (Natl. Univ. Cordoba, Argentina). *Rev. Esp. Enferm. Apar. Dig.* 39(4):365-376, 1973.

See also, 6428, 6482, 6484, 6500, 6508, 6712, 6718, 6721, 6728, 6741, 6756, 6837, 6856, 6867, 6885, 7114, 7161, 7201, 7264, 7275, 7532, 7565, 7577, 7591, 7598, 7624, 7689, 7727, 7749, 8037, 8165, 8237.

GENERAL

8011 PARADOXICAL EFFECT OF SECRETIN ON SERUM IMMUNOREACTIVE GASTRIN IN THE ZOLLINGER-ELLISON SYNDROME. *(E.)* Korman, M. G.; Soveny, C.; Hansky, J. (Prince Henry's Hosp., Melbourne, Australia). *Digestion* 8(5):407-416, 1973.

Serum gastrin was measured by radioimmunossay following i.v. secretin in 86 control subjects, 9 patients with pernicious anemia, and 9 patients with Zollinger-Ellison syndrome. In 55 control subjects, Boots secretin (2 U/kg) produced a significant fall in serum gastrin from 40 to 17 pg/ml; in 31 control subjects, GIH secretin (1 U/kg) produced a significant fall from 41 to 14 pg/ml. In the 9 patients with pernicious anemia both injection and infusion of Boots secretin caused a significant fall in serum gastrin, 1,030 to 360 pg/ml and 1,055 to 310 pg/ml, resp. Of 9 patients with Zollinger-Ellison syndrome, Boots secretin caused a substantial rise in serum gastrin in 6 and no change in the other 3. It is suggested that secretin inhibits gastrin release from antral cells and stimulates its release from islet cell tumours; this paradox may have diagnostic application in the Zollinger-Ellison syndrome.

8012 BALANCE STUDIES IN AN INFANT WITH CONGENITAL CHLORIDE DIARRHEA. *(Ger.)* Bremer, D.; Heinisch, H. M. (Pediatric Clin., Univ. Cologne, Germany). *Monatsschr. Kinderheilkd.* 121(7):403-405, 1973.

Because of dyspepsia and low water intake, a newborn infant with a birth weight of 2320 g lost 340 g during the first 4 days of life. The child developed hyperbilirubinemia (maximum of 10.5 mg/100 ml bilirubin), alkalosis, and chronic diarrhea which was refractory to treatment. The fecal chloride concentration was 10 times higher (169 mEq/liter) than normal, while the dry weight of the stool was only 1/10 of normal values; concentrations of sodium and potassium were about the same as in other forms of diarrhea. Treatment consisted of adding 3 g/day of sodium chloride to the diet. When this salt was gradually withdrawn at age 7 months, the infant's condition rapidly became worse. Serum potassium and chloride decreased significantly, the blood pH increased to 7.61 and serum bicarbonate to 40 mEq/liter, while the partial pressure of carbon dioxide remained normal. At 8 months the patient did well when given 0.5 g/kg/day of sodium chloride. Since the infant omited when given potassium chloride, he was fed a igh-potassium diet. As has been found in other ases of chloride diarrhea, there was a maternal istory of hydramnios. However, this infant was orn to Turkish parents (chloride diarrhea is most ommon in Finland) and there was no familial history f chloride diarrhea.

013 HEREDITARY HEMORRHAGIC TELANGIECTASIA IN A BLACK FAMILY. *(E.)* Bryan, C. S. (Vanderilt Univ. Med. Ctr., Nashville, Tenn.). *Am. J. ig. Dis.* 18(10):912-914, 1973.

igmoidoscopic examination disclosed red vascular esions described as polypoid or hemangiomatous in n 18-yr-old black woman suffering from chronic inestinal bleeding. Intestinal bleeding during the irst pregnancy at age 22 was attributed to iron-lack nemia. At age 26, during the third pregnancy, leeding recurred. At age 27, following tooth exraction, she became febrile. Blood cultures yielded *treptococcus viridans* for which penicillin proved ccessful treatment. Her maternal grandfather was iagnosed with hereditary hemorrhagic telangiectasia t age 60 yr. By 71 yr, he had widespread telaniectases on the lips, buccal mucosa, and tongue. nexplained gastrointestinal bleeding caused hospitalzation of 3 of her maternal uncles. A maternal aunt d iron-lack anemia of unknown origin at age 42. f 2 brothers, 1 had recurrent epistaxis. Her ther had had a history of recurrent epistaxis. t is stressed that the disease may be overlooked n blacks due to difficulty in recognizing cutaneous elangiectases, and it is suggested that a thorough earch for telangiectasia should be made in any black th gastrointestinal bleeding. When no evidence of elangiectases is seen on the palms, nailbeds, r oronasal mucosa, it is advisable to examine older mily members.

14 THE VALUE OF IMMUNOLOGY IN THE STUDY OF GASTROINTESTINAL CANDIDIASIS (IMMUNOELECOPHORESIS AND INDIRECT IMMUNOFLUORESCENCE). *(Fr.)* ris, J.; Capron, A.; Vernes, A.; Paris, J. C.; drieu, S. (Univ. Hosp. Ctr., Lille, France). *ch. Fr. Mal. App. Dig.* 62(4):309-313, 1973.

tibodies to *Candida albicans* were determined by direct immunofluorescence and immunoelectrophores in serum from 69 patients with large numbers of pe A or B *C. albicans* in their stools. These paents included 11 who had been given antibiotics, diabetics, 28 with hepatic insufficiency, and with a variety of gastrointestinal symptoms; 1 tient had *C. albicans* septicemia. Forty subjects o had *C. albicans* in their stools but were asympmatic served as controls. At dilutions of 1:200 higher none of the controls and 62.6% of the paents had immunofluorescent antibodies to *C. bicans*; 66.5% of the patients had precipitating tibodies on electrophoresis. These findings conrm that the sensitivities of indirect immunofluescence and immunoelectrophoresis are about the me for detecting antibodies to *C. albicans*.

One system of antibodies, called A, which were associated with chronic symptoms, was present in 94% and another system, called B, which occurred in acute cases and were associated with strongly positive reactions for immunofluorescent antibodies, was present in 49% of the patients with precipitating antibodies on electrophoresis. Clinical improvement occurred and blood cultures became negative when a man with *C. albicans* septicemia was given 90 mg of amphotericin B i.v. over a 10-day period, but *C. albicans* was still cultured from his stools. When symptoms of partial intestinal obstruction developed, this patient underwent laparotomy and encysted peritonitis was diagnosed. The patient then developed bladder symptoms, and *C. albicans* was detected in his urine; a small thoracic abscess was found which also contained *C. albicans*. On immunoelectrophoresis, precipitating antibodies to *C. albicans* were detected at dilutions as high as 1:3200.

8015 THE EFFECTS OF INTRAVENOUS AND INTRADUODENAL FEEDING ON NITROGEN BALANCE AFTER SURGERY. *(E.)* Hindmarsh, J. T.; Clark, R. G. (Nova Scotia Inst. Pathol., Halifax, Canada). *Br. J. Surg.* 60(8): 589-594, 1973.

To assess the value of nutrition in the first week after surgery, total nitrogen balance was determined in 3 groups of patients (2 experimental, 1 control) undergoing vagotomy and pyloroplasty from 1 day before to 8 days after operation. In the experimental groups nutrition was maintained postoperatively by the i.v. route in 8 patients and intraduodenally in another 7 at a level adequate for normal nonpostoperative subjects. Water and electrolyte intakes were similar in the 3 groups, but the 11 patients in the control group received no calories or nitrogen in the immediate postoperative period. With respect to nitrogen economy, the group fed largely by the intraduodenal route fared best. Nevertheless, nitrogen balance did not reach equilibrium until day 5 in any group, probably indicating a relative increase in protein catabolism in the early postoperative period. In all groups only small amounts of carbohydrate were recovered from the urine, and sodium and potassium losses in gastric aspirates were slight as were sodium, potassium, and fat losses in the feces.

8016 STRUCTURE AND FUNCTION OF THE GASTROINTESTINAL TRACT IN PRIMARY IMMUNODEFICIENCY SYNDROMES. A STUDY OF 39 PATIENTS. *(E.)* Ament, M. E.; Ochs, H. D.; Davis, S. D. (Univ. Washington Sch. Med., Seattle). *Medicine* 52(3):227-248, 1973.

Abnormalities in gastrointestinal structure, function, and symptoms were studied in 39 patients (28 males and 11 females, aged 1 1/2 to 53 yr) with various immunodeficiency syndromes. Gastrointestinal symptoms, abnormalities in villus structure, and absorptive dysfunction were present in 9. In all but 1 individual, giardiasis was the cause of gastrointestinal illness. Among the 30 asymptomatic individuals, only 3 had giardiasis. Multiple small bowel biopsies were needed to assess the morphology in every symptomatic case because the villus architecture varied greatly in the same individual at different times. Treatment with metronidazole reversed steatorrhea, lactose intolerance, disaccharidase deficiency, and protein losing enteropathy. Vitamin B_{12} absorption was abnormal in all giardiasis patients. Bacterial overgrowth with coliforms was frequently observed, but did not appear to correlate with gastrointestinal symptoms, malabsorption, or intestinal lesions. Asymptomatic patients without giardiasis did not have steatorrhea. In patients with ataxia-telangiectasia and variable immunodeficiency syndrome, mild vitamin B_{12} malabsorption unrelated to giardiasis was noted. The recurrence of diarrhea was noted in 2 patients categorized as having variable immunodeficiency syndromes 1 yr after their initial illness and in each case this was attributed to colitis. Morphologic evidence of colitis was seen in rectal biopsy from 9 asymptomatic patients whose rectal mucosa appeared normal by sigmoidoscopy. These histologic changes may represent a compensatory mobilization of intact defense mechanisms in immunologically deficient patients. It is concluded that abnormalities in intestinal structure and function in immunodeficiency syndromes are secondary to giardiasis and are seen almost exclusively in patients with variable immunodeficiency syndrome. The existence of severe malabsorption with a flat intestinal lesion in 1 variable immunodeficiency syndrome patient remains unexplained.

8017 GASTROINTESTINAL MASTOCYTOSIS: PRESENTATION OF ONE CASE AND REVIEW OF THE LITERATURE.

(Fr.) Debray, C.; Leymarios, J.; Cerf, M.; Bocquet, L.; Marche, C.; Boivin, P.; Kahn, A.; Husson, J. M. (Bichat Hosp., Paris, France). *Arch. Fr. Mal. App. Dig.* 62(5):411-417, 1973.

A 46-yr-old man with urticaria pigmentosa, severe anemia, episodes of facial flushing, and hepatosplenomegaly had a 2-yr history of diarrhea but normal D-xylose tests and subnormal fecal fat excretion. X-ray examinations revealed round defects in the stomach, duodenum, jejunum, and colon and moderate thickening of the jejunal folds. Biopsies of the duodenum and jejunum showed partial villous atrophy, infiltrations of plasma and lymph cells in the lamina propria, a large increase in the size of duodenal glands, and an increase in the number of goblet cells in the jejunum; few mast cells were found in the infiltrates at this time. No IgA was detected in the intestinal contents. Administration of a soluble derivative of prednisolone and an antihistamine (tavegil) produced no clinical improvement, and the patient died with an exacerbation of anemia and cachexia 4 yr after onset of diarrhea. Autopsy revealed mast cell infiltration of the liver with tumor nodules in the portal spaces and parenchyma; fibrosis was moderate. Mast cell infiltrates were also present in the heart, lumbar and aortic lymph nodes, bone marrow, and spleen.

8018 HYDATID CHOLEPERITONEUM AND PYOPERITONEUM (ABOUT TWO CASES).

(Sp.) Ferreira Montero, V.; Fabian, P. G. (Jose Antonio Munic. Sanitorium, Zaragoza, Spain). *Rev. Esp. Enferm. Apar. Dig.* 39(5) 589-594, 1973.

Case reports are presented for 2 women, aged 63 and 44 yr, who developed peritonitis from the rupture of large hydatid cysts of the liver. Both patients had long histories of "biliary colic" and jaundice although radiological examination of the younger woman was negative. The older woman presented with acute and persistent abdominal pain accompanied by fever, nausea, vomiting, profuse sweating, and a WBC of 19,900. The younger woman presented with pain in the right hypochondrium, a mass occupying the entire hypochondrium, fever, and jaundice. A tentative diagnosi of hydatid cyst was established. At laparotomy the abdomens of both patients were filled with large quantities of pus mixed with bile and hydatid vesicle The older woman had a perforated hydatid cyst of the left lobe of the liver and another unperforated cyst, measuring 3 cm in diameter, in the greater omentum. The younger woman had a perforated hydatid cyst in the right lobe of the liver. In both cases surgery consisted of draining and cleaning out the abdominal cavity and marsupialization of the ruptured cyst; the small cyst in the greater omentum of the older woman was removed. In the older woman the post operative course was complicated by dehiscence of the incision which necessitated repair. The younger woman went into septic shock immediately after surgery but responded to therapy. Both patients are alive and well 5 months and 3 yr, resp., after surgery.

8019 EPITHELIAL MUCINS IN GASTROINTESTINAL CARCINOIDS: HISTOCHEMICAL STUDY OF 29 CASES.

(Fr.) Schoetter, F.; Weill-Bousson, M. (Inst. Hyg. Public Health, Luxembourg). *Ann. Anat. Pathol. (Paris)* 17(2):161-176, 1972.

The histochemistry of epithelial mucins was investig in 29 gastrointestinal carcinoids and 20 mucous-secr ting columnar epitheliomas of the gastrointestinal tract. Carcinoids consisted of 14 in the appendix, 10 in the small intestine, 4 in the large intestine, and 1 in the stomach; 3 had metastasized to the lymp nodes, 4 to the liver, and 1 to the ovary. Associat adenocarcinomas were found in 1 patient with an appendiceal carcinoid and in 1 with a carcinoid of the small intestine. Of these 29 carcinoids, 25 contain argentophilic granules and 22 (75%) contained acini which stained with periodic acid-Schiff (PAS) reagen and alcian blue at pH 2.5. Most of these acini also gave positive reactions with colloidal iron, Gomori' aldehyde-fuchsin, alcian blue/PAS, and mucicarmine, demonstrating that the substance inside these acini was epithelial mucus consisting of a mixture of neutral and weakly acidic mucins, including carboxymuci and sialomucins; little or no sulfomucin was present These findings were not specific for carcinoid mucus since mucus from columnar epitheliomas had essentially the same composition but did contain, in additio some sulfomucin. Mucus was present only at the apical pole of the cells in both types of tumors. In cells adjacent to the acini a thin, apical border was sometimes also stained with PAS, alcian blue at pH 2.5, colloidal iron, and Gomori's aldehyde-fuchsin. In some carcinoids fine particles of glycogen were PAS-positive, but their color disappeared with salivary amylase. Acini were found in larger numbers in carcinoids of the small intestine and colon than in carcinoids of the appendix. Large numbers of mucous-secreting acini were found in the submucosa, but they were also present in the muscularis and subserosa. Acini were also present in all the metastases examined. No other mucous-secreting structures were found.

8020 AMINO ACID ADEQUACY OF PARENTERAL CASEIN HYDROLYSATE AND ORAL COTTAGE CHEESE IN PATIENTS WITH GASTROINTESTINAL DISEASE AS MEASURED BY NITROGEN BALANCE AND BLOOD AMINOGRAM.

(E.) Patel, D.; Anderson, G. H.; Jeejeebhoy, K. N. (Toronto, Gen. Hosp., Ontario, Canada). *Gastroenterology* 65(3):427-437, 1973.

Nitrogen retention with i.v. casein hydrolysate (0.25, and 0.5, and 1.0 g/kg) was compared to nitrogen retention with oral casein hydrolysate and oral cottage cheese in 12 malnourished patients. Diagnoses in these 12 included: malabsorption syndrome with agammaglobulinemia (1); total gastrectomy with alkaline esophagitis (3); total gastrectomy for Zollinger-Ellison syndrome, anastomotic obstruction and fistula (1); recurrence of Crohn's disease and malabsorption (1); esophageal fistula (1); peritonitis (1); duodenal fistula (1); and portacaval shunt and cirrhosis of the liver (3). The route by which casein hydrolysate was adminstered did not significantly influence nitrogen retention. Oral cottage cheese induced superior nitrogen retention when compared to i.v. or oral casein hydrolysate. Blood amino acid studies indicated that poor nitrogen retention with casein hydrolysate in patients capable of retaining nitrogen, when a high quality protein was fed p.o., was due to an imbalance of amino acids in the hydrolysate. Casein hydrolysate was found to have a relative deficiency of sulfur and aromatic amino acids and an excess of valine and lysine. In practical terms, these studies imply that oral cottage cheese is a superior source of amino acids than casein hydrolysate and there is no place for using casein hydrolysate intravenously to "build up" patients who are capable of ingesting cottage cheese.

8021 TRANSIENT BACTEREMIA ASSOCIATED WITH SIGMOIDOSCOPY.

(E.) LeFrock, J. L.; Ellis, . A.; Turchik, J. B.; Weinstein, L. (Tufts-New ngland Med. Ctr. Hosp., Boston, Mass.). *N. Engl. J. ed.* 289(9):467-469, 1973.

outine sigmoidoscopic examinations were performed on 00 patients hospitalized for diverse reasons. None ad received antimicrobial agents during the 6 months efore hospitalization. The patients were separated nto 2 groups: 106 patients with no history of lower astrointestinal disease and 94 patients with a varety of lower gastrointestinal disorders. Venous blood samples (in series) were taken before and after sigmoidoscopy. The standard rigid sigmoidoscope was used, and examination of almost all patients extended to 25 cm. Although no patient had demonstrable bacteremia before sigmoidoscopy, 19 patients (9.5%) showed bacteremia after the procedure. Of these, 9 (8.5% of 106) had no evidence of lower intestinal disease and 10 (10.6% of 94) had active disease of the lower intestinal tract. The presence of lower intestinal disease did not significantly affect the incidence of bacteremia. Analysis of data indicated that routine sigmoidoscopy is associated with true transient bacteremia, beginning, in some cases, within the first min after the procedure and lasting for as long as 15 min. Disparity between these results and those of other studies may be due to increased frequency of sampling in this study or to the use of the pour-plate method of blood culture.

8022 RADIOIMMUNOLOGIC MEASUREMENTS OF NATURALLY OCCURRING BACTERIAL ANTIBODIES. I. HUMAN SERUM ANTIBODIES REACTIVE WITH ESCHERICHIA COLI IN GASTROINTESTINAL AND IMMUNOLOGIC DISORDERS.

Brown, W. R.; Lee, E. M. (VA Hosp., Denver, Colo.). *J. Lab. Clin. Med.* 82(1):125-136, 1973.

A radioimmunologic method for quantitative measurement of naturally occurring human serum antibodies reactive with *Escherichia coli* was developed. From measurements of radiolabeled rabbit antihuman immunoglobulins bound to bacteria which had been incubated in human serum or purified immunoglobulins, the primary binding of IgG, IgA, and IgM to a nonenteropathogenic strain of *E. coli* was estimated. As little as 5 ng antibody nitrogen could be measured. No significant interference was encouraged from cross-reacting antibodies to *Bacterioides fragilis*, an *Enterococcus* species, or human erythrocytes. In sera of 11 healthy subjects and 72 patients with immunologic or gastrointestinal disorders; anti-*E. coli* were measured, IgM and IgG antibodies predominated quantitatively over IgA antibodies. Antibody concentrations were normal in many gastrointestinal conditions in which elevations might have been expected (nontropical sprue, regional enteritis, intestinal bacterial overgrowth, syndrome and postnecrotic cirrhosis. IgG antibodies were undetectable in sera of 3 of 8 patients with chronic ulcerative colitis, the only patients in the entire series except for those with hypogammaglobulinemia in whom this was observed. IgG antibody concentrations were 2 to 17 times above the maximum normal control value in 4 of 10 patients selectively deficient in IgA; and IgA class antibodies were below measurable levels in all 20 IgA myeloma sera. This radioimmunoassay method has proved useful for measurement of naturally occurring anti-*E. coli* antibodies and should be applied to the study of antibodies to other bacteria.

8023 ACUTE INFECTIOUS NONBACTERIAL GASTROENTERITIS: INTESTINAL HISTOPATHOLOGY. HISTOLOGIC ENZYMATIC ALTERATIONS DURING ILLNESS PRODUCED BY THE NORWALK AGENT IN MAN.

(E.) Agus, S. G.; Dolin,

R.; Wyatt, R. G.; Tousimis, A. J.; Northrup, R. S. (Natl. Inst. Health, Bethesda, Md.). *Ann. Intern. Med.* 79(1):18-25, 1973.

Intestinal biopsy specimens were obtained from 7 normal volunteers (all male, aged 19-21 yr) before, during, and after administration of the Norwalk agent of acute infectious nonbacterial gastroenteritis. Of the volunteer, 4 became acutely ill with 3 having diarrhea, 2 vomiting, 2 low-grade fever, 3 abdominal cramps, and 3 headache. The incubation period of the illness was 16-36 hr; duration was 24-48 hr. The small intestine of the 4 ill volunteers had an intact mucosa but showed histologic changes that included blunting of villi, shortening of microvilli, dilation of endoplasmic reticulum, and an increase in intracellular multivesiculate bodies. Convalescence biopsy specimens, obtained 2 weeks after illness, showed normal histologic patterns. Specimens obtained from volunteers who remained clinically well did not show histologic changes at any time. At the time of illness, brush-border enzyme activities (alkaline phosphatase, sucrase, and trehalase) were decreased as compared with base-line and convalescent values. Thus, definite but reversible pathophysiologic lesions of the small intestine in man were seen during acute gastroenteritis induced by a viral agent.

8024 THE JEJUNAL MUCOSA IN PROTEIN-ENERGY MALNUTRITION. A CLINICAL, HISTOLOGICAL, AND ULTRASTRUCTURAL STUDY. *(E.)* Shiner, M.; Redmond, A. O. B.; Hansen, J. D. L. (Dept. Pediatr., Univ. Witwatersrand, Johannesburg, South Africa). *Exp. Mol. Pathol.* 19(1):61-78, 1973.

The jejunal mucosa of 5 children with kwashiorkor type of protein-energy malnutrition was studied by histological and fine structural techniques before and after treatment. In the 3 most severely ill patients, in whom a subtotal mucosal atrophy was found, the ultrastructural appearances of the absorptive cells and the endothelium showed a decrease in endoplasmic reticulum, dilated vesicles, and numerous vacuoles probably of phagocytic type. These changes responded to treatment that included i.v. fluids, plasma and blood, oral penicillin, sulfonamide, and various oral nutritional supplements. However, the advisability of oral feeding is questioned in cases where severe structural abnormalities are found, for the mucosa may be unable to cope with the absorption of food presented via the bowel lumen. Thus, systemic feeding is suggested in the early stages of severe protein-energy malnutrition.

8025 ELEMENTAL DIET IN THE TREATMENT OF FISTULAS OF THE ALIMENTARY TRACT. *(E.)* Voitk, A. J.; Echave, V.; Brown, R. A.; McArdle, A. H.; Gurd, F. N. (Montreal Gen. Hosp., Canada). *Surg. Gynecol. Obstet.* 137(1):68-72, 1973.

Elemental diet was used to treat 29 patients with 36 fistulas located in the esophagus (2), stomach and duodenum (3), small intestine (17), colon (6), and pancreatic and biliary tract (8). Five of the fistulas were created to drain pancreatic pseudocysts, and 10 fistulas developed as a result of the patient's disease; the remaining 21 occurred as a surgical complication. Of these 29 patients, 8 (28%) died. Death was attributed to metastatic cancer in 4 patients and to pancreatitis in 1 patient. If patients with metastatic cancer are excluded, the mortality for this series would be 16%. Three deaths were caused by the fistula or its complications, with malnutrition and sepsis as important factors contributing to these 3 deaths. There were 10 fistulas in the 8 patients who died; 7 were open at the time of death. Among the survivors, 1 was unable to tolerate the elemental diet and another had a fistula which remained open, because of persistent obstruction distal to the duodenum, despite 3 attempts to close it surgically. The remaining 27 fistulas closed spontaneously after treatment with elemental diet. Measurements of changes in nitrogen balance and red cell mass showed that the elemental diet effectively supplied the nutritional needs of the depleted, healing body without aggravating the fistula by corrosive fecal drainage.

8026 SURGICAL COMPLICATIONS OF NEONATAL NECROTIZING ENTEROCOLITIS. *(E.)* Kosloske, A. M.; Martin, L. W. (Coll. Med., Univ. Cincinnati, Ohio). *Arch. Surg.* 107(2):223-228, 1973.

8027 EPIDEMIOLOGY AND COURSE OF GASTROINTESTINAL HAEMORRHAGE IN NORTH-EAST SCOTLAND. *(E.)* Johnston, S. J.; Jones, P. F.; Kyle, J.; Needham, C. D. (Aberdeen Roy. Infirm., Scotland). *Br. Med. J.* 3(5882):655-660, 1973.

8028 FURTHER HAEMORRHAGE AFTER ADMISSION TO HOSPITAL FOR GASTROINTESTINAL HAEMORRHAGE. *(E.)* Jones, P. F.; Johnston, S. J.; McEwan, A. B.; Kyle, J.; Needham, C. D. (Foresterhill Hosp., Aberdeen, Scotland). *Br. Med. J.* 3(5882):660-664, 1973.

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8031 STUDY OF THE COMBINATION OF A NEUROLEPTIC AND ANTICHOLINERGIC AGENT IN GASTROENTEROLOGY: 44 CASES. *(Fr.)* Cain, D. (no affil.). *Gaz. Med. France* 80(12):2123-2128, 1973.

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Fr.) Cadudal, J. L.; Nicolas, F.; Mainard, R.;
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rislain, J. R. (Hosp. Ctr., Univ. Nantes, France).
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oussy Inst., Villejuif, France). *Arch. Anat. Pathol.
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eyer-Cleempoel, S. (St. Raphael Univ. Hosp.,
uvain, Belgium). *Arch. Belg. Med. Soc.* 30(4):
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nfils, S. (Bichat Hosp., Paris, France). *Arch.
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ept. Microbiol., Southern Illinois Univ.,
rbondale). *Arch. Gesamte Virusforsch.* 42(1):78-
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39 EXPERIMENTAL STUDIES ON CHOLERA IMMUNISATION: THE PROTECTIVE IMMUNOGENICITY IN
BBITS OF MONOMERIC AND POLYMERIC CRUDE EXOTOXIN.
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8129 CONSIDERATIONS OF HYPONATRAEMIA CONVULSIONS IN THE COURSE OF SEVERE INFANTILE DIARRHOEA. *(E.)* Priscu, R.; Maiorescu, M.; Anca, I.; Georgescu, A.; Wirtz, A.; Iordanescu, A. ("Emilia Irza" Clin. Paediatr., Bucharest, Romania). *Rom. Med. Rev.* 17(2): 61-65, 1973.

8130 INTESTINAL HEMANGIOMATA IN CHILDHOOD AND A SYNDROME FOR DIAGNOSIS: A COLLECTIVE REVIEW. *(E.)* Abrahamson, J.; Shandling, B. (Hosp. Sick Children, Toronto, Canada). *J. Pediatr. Surg.* 8(4):487-495, 1973.

8131 FATAL DIARRHOEAL DISEASE IN AUSTRALIAN ABORIGINAL CHILDREN. *(E.)* Gracey, M.; Bower, G. (Princess Margaret Children's Med. Res. Fdn., Perth, Australia). *Aust. N.Z. J. Med.* 3(3):255-259, 1973.

8132 OBSERVATIONS ON THE ECOLOGY OF ENTEROVIRUSES IN POLAND. *(E.)* Kantoch, M.; Magdzik, W.; Glowacka, A.; Dobrowolska, H. (State Inst. Hyg., Warsaw, Poland). *Epidemiol. Rev.* 26(3):311-317, 1972.

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8134 DEVELOPMENT OF THE SEVENTH CHOLERA PANDEMIC. *(E.)* Naruszewicz-Lesiuk, D. (State Inst. Hyg., Warsaw, Poland). *Epidemil. Rev.* 26(3):340-345, 1972.

8135 CHRONIC AND RECURRENT DIARRHEA IN AMERICAN SERVICEMEN IN VIETNAM. AN EVALUATION OF ETIOLOGY AND SMALL BOWEL STRUCTURE AND FUNCTION. *(E.)* Butler, T.; Middleton, F. G.; Earnest, D. L.; Strickland, G. T. (Naval Support Activity Sta. Hosp., Danang, South Vietnam). *Arch. Intern. Med.* 132(3): 373-377, 1973.

8136 MINOR SALIVARY GLAND TUMORS. *(E.)* Stimson, P. G. (Univ. Texas Dental Br., Houston). *Cancer Bull.* 25(5):92-101, 1972.

See also, 6194, 6378, 6381, 6709, 6739, 6792, 6794, 6807, 6817, 6840, 6853, 6870, 6887, 6888, 6923, 7078, 7121, 7218, 7262, 7303, 7334, 7398, 7511, 7525, 7600, 7613, 8047, 8223.

GENERAL

Parasitology

8137 HISTOPATHOLOGICAL AND RADIOLOGICAL APPEARANCES OF DUODENUM IN GIARDIASIS- A PRELIMINARY REPORT. *(E.)* Nath, S.; Chawla, L. S.; Sehgal, A. K.; Grewal, M. S.; Broor, S. L. (Postgrad. Inst. Med., Chandigarh, India). *Bull. Postgrad. Inst. Med. Ed. Res.* 6(4):178-181, 1972.

To determine whether there is any correlation between histological and radiological features in giardiasis, duodenal biopsies were taken and barium examinations made on 23 patients with parasites present in their stools and duodenal aspirates. The height of the villi was normal in 10 and decreased in 13 of these patients. The cell count was increased in the lamina propria in 20 (87%), and infiltration of the mucosal epithelium occurred in 12 (52%). A correlation was found between the increased mitotic index, found in 22 cases, and the severity of the abnormality. The changes observed were similar to those found in the jejunum in giardiasis. Radiological examinations showed that mucosal fold thickness was increased in 19 cases, and increased duodenal irritability was present in 17. A significant negative correlation was found between the height of the villi and the mucosal fold thickness. After treatment mucosal fold thickness was increased in 6 patients, and increased duodenal irritability was present in only 3.

8138 THE CLINICAL PATTERN AND PROGNOSIS OF PATIENTS WITH AMEBIC LIVER ABSCESS AND JAUNDICE. *(E.)* Datta, D. V.; Saha, S.; Singh, S. A.; Aikat, B. K.; Chhuttani, P. N. (Postgrad. Inst. Med. Ed. Res., Chandigarh, India). *Am. J. Dig. Dis.* 18(10):887-898, 1973.

undice occurred in 27 (25 males and 2 females, aged
-76 yr) of 95 patients with amebic liver abscess
spitalized over a 5-yr period. Serum bilirubin
vels ranged from 2 to 31 mg/100 ml. The conjugated
action invariably predominated. Patients with
undice had a shorter duration of illness, more fre-
ent error in their initial diagnosis, a higher in-
dence of complications, and a higher mortality rate
en compared to patients without jaundice. At ne-
opsy these patients had abscesses that were either
the inferior surface of the liver where main bile
ct tributaries emerge or were of such a dimension
to compress this region. It is concluded that
undice is of cholestatic origin due to compression
destruction of main intrahepatic biliary channels.
is extremely important that the possible presence
jaundice be recognized, a diagnosis be established
rly, and an effective aspiration carried out in
tients with amebic liver abscess.

39 QUANTITATIVE STUDY OF P SUBSTANCE IN THE
MEGAESOPHAGUS AND MEGACOLON OF HUMAN TRY-
NOSOMA CRUZI INFECTIONS. *(E.)* Hial, V.; Diniz,
R.; Pittella, J. E. H.; Tafuri, W. L. (Inst.
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ophageal and colon fragments from 31 surgical
tients (12 females and 19 males, aged 4-77 yr)
th trypanosomiasis were examined histologically.
inical and pathological diagnoses included
uamous cell carcinoma (6), adenocarcinoma (7),
agasic megaesophagus (13), lymphosarcoma (1),
ronic miliary schistosomiasis (1), nonspecific
ronic enterocolitis (1), and colon without
ident histologic changes (1). Histological
anges included: (1) periganglionitis, ganglioni-
s, perineuritis, and focal or diffuse chronic
uritis, total or partial fibrosis of the nervous
ructure and subsequent reduction in the number
neurons; (2) focal chronic myositis in the thick-
ss and along muscle layers; fibrosis in the
tracellular spaces and among bundles of muscle
lls; and (4) chronic inflammatory infiltration
the corium and muscle layer. No evidence of
ishmania was observed. The levels of P substance
the megaesophagus and megacolon of the patients
d not differ significantly from levels in a
ntrol group. It is suggested that in patients
th trypanosomiasis, neurons which are not destroyed
ep on synthesizing and/or storing P substance in
rger than normal amounts, perhaps because of some
rt of compensatory mechanism. This is supported
an increase in the number and volume of large
anular vesicles, where neurotransmitter substances
e found.

40 GIARDIASIS AND COELIAC DISEASE. *(E.)*
Carswell, F.; Gibson, A. A. M.; McAllister,
A. (Roy. Hosp. Sick Children, Glasgow, Scotland).
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e incidence of *Giardia lamblia* infestation, as
own by examination of the stools, is the same in
normal and celiac children. In 93 patients who were suspected of having celiac disease, upper intestinal biopsies were examined for giardia infestation. These patients usually had at least 1 stool and/or duodenal juice sample examined for *G. lamblia*. Giardiasis occurred in 26 patients (14 celiac, 12 nonceliac). Only 13 patients would have been diagnosed if stools alone had been examined. Patients with giardiasis were usually male, younger than the other patients, more likely to have concurrent bacterial infection in the bowel, and more likely to come from a lower socioeconomic group. When the jejunal biopsies of 57 celiac patients, including those with and without giardiasis, were compared, *G. lamblia* were more commonly found in those patients with less severe histological changes.

8141 QUANTITATIVE STUDY OF MAST CELLS IN THE ESOPHAGEAL MUSCULATURE IN SUBJECTS WITH CHRONIC TRYPANOSOMIASIS. *(Por.)* Pereira, F. E. L. (Fac. Med., Fed. Univ., Espirito Santo, Brazil). *Rev. Inst. Med. Trop. Sao Paulo* 14(1):30-32, 1972.

After fixation in 10% formol, a ring was removed from the middle 1/3 of the esophagus, embedded in paraffin, stained with 0.5% toluidine blue at pH 4, and mounted in water. Material was obtained from the esophagi of 20 subjects, aged 18-65 yr, with negative Guerreiro-Machado tests for trypanosomiasis and 20 subjects, aged 14-60 yr, with positive Guerreiro-Machado tests but with no evidence of megaesophagus. The mean number of mast cells, determined in 20 microscope fields, was 243 for individuals with chronic trypanosomiasis and 145.8 for controls without trypanosomiasis. Although specimens were fixed at various periods after death, the results appear valid since literature reports indicate there are only slight differences in the number of mast cells in organs fixed 10 hr after death and in those fixed after 24 hr when autolysis has occurred. Since mast cells appear to be related to fibrinogenesis, this increase in the number of mast cells in trypanosomiasis may be related to the increase in interstitial collagen.

8142 EXPERIMENTAL TRICHINOSIS. III. INTESTINAL TRANSPLANTATION OF ADULT TRICHINELLA SPIRALIS. *(Fr.)* Mougeot, G.; Lancastre, F. (Fac. Med., Paris-St. Antoine, France). *Ann. Parasitol. Hum. Comp.* 48(1):55-59, 1973.

8143 INTESTINAL PARASITIC DISEASES. PROBLEMS OF PUBLIC HEALTH IN REUNION. *(Fr.)* Lariviere, M.; Picot, H.; Languillat, G.; Beauvais, B.; Therizol, M.; Coumbaras, A. (Teaching Res. Unit Lariboisiere-St. Louis, Paris, France). *Ann. Parasitol. (Paris)* 48(2):249-262, 1973.

8144 CLINICAL TRIAL WITH THIABENDAZOLE IN INTESTINAL HELMINTHIC INFESTATION IN CHILDREN. *(E.)* Wakhlu, I.; Sharma, N. L.; Singh,

N. P. (K.G. Med. Coll., Lucknow, India). *Arch. Child Health* 14(3):118-121, 1972.

8145 SOME REFLECTIONS OF BLOOD AND INTESTINAL PARASITES IN TWO VILLAGES IN CENTRAL AFRICA. *(Fr.)* Brumpt, L. C.; Ho, T. S.; Jaeger, G. (Necker-Enfants Malades Univ. Hosp. Ctr., Paris, France). *Bull. Soc. Pathol. Exot.* 65(2):263-270, 1972.

8146 POSTAMEBIC DISEASES OF THE COLON. (FIFTY CASES). *(Fr.)* Pene, P.; Gastaut, J. A. (M. A. F. F. Central Vet. Lab., New Haw, Weybridge, Surrey, England). *Bull. Soc. Pathol. Exot.* 65(5): 656-663, 1972.

8147 MEGENDAZOLE, A NEW ANTHELMINTIC, VERY ACTIVE AGAINST A LARGE SPECTRUM OF TRICHOCEPHALUS. *(Fr.)* Vandepitte, J.; Lontie, M.; Krubwa; Nguete-Kikhela; Thienponi, D. (St. Raphael Univ. Hosp., Leuven, Belgium). *Bull. Soc. Pathol. Exot.* 66(1): 165-178, 1973.

8148 AN EXPERIENCE WITH METRONIDAZOLE (FLAGYL) IN GIARDIASIS IN CHILDREN. *(E.)* Bhatia, S. M.; Kharod, M. J. (L. G. Gen. Hosp., Ahmedabad, India). *Indian Pract.* 26(3):139-142, 1973.

8149 MORPHOLOGICAL AND FUNCTIONAL CHANGES IN THE GASTRIC MUCOSA IN PATIENTS IN THE EARLY STAGE OF OPISTHORCHIASIS. *(Rus.)* Mel'nikov, V. I.; Ginovker, A. G.; Skarednov, N. I. (Tiumen Med. Inst., USSR). *Med. Parazitol. (Mosk.)* 41(4):391-393, 1972.

8150 CLINICAL AND PARASITOLOGICAL EVALUATION OF THE THERAPEUTIC EFFECTIVENESS OF A NEW CHEMOTHERAPEUTIC AGENT (NIFURATEL) IN THE TREATMENT OF INTESTINAL AMEBIASIS. *(Por.)* de Figueiredo, J. A. (Penetentiary Hosp., Sao Paulo State, Brazil). *Rev. Bras. Clin. Ter.* 2(7):303-310, 1973.

8151 INTESTINAL PARASITES IN A GENERAL PEDIATRICS DEPARTMENT. (STATISTICS FOR 12 YEARS). *(Fr.)* Lelong, M.; Deroubaix, P.; Derambure, S.; Sorez, J. P.; Vanlaeys, R.; Thelliez, P.; Hogedez, G. (no affil.). *Lille Med.* 18(4):430-432, 1973.

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8194 A COMPARISON OF STOOL EXAMINATION AND MASS-TREATMENT FOR INDICATION OF THE PREVALENCE OF TAENIA SAGINATA. *(E.)* Farahmandian, I.; Sahba, G. H.; Arfaa, F.; Movafagh, K. (Sch. Public Health, Univ. Teheran, Iran). *Trop. Geogr. Med.* 25(2):171-173, 1973.

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8198 TINIDAZOLE IN AMOEBIASIS. *(E.)* Zuberi, S. J.; Ibrahim, M. (Pakistan Med. Res. Council, Karachi). *Practitioner* 211(1261):93-95, 1973.

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8203 SOME CLINICAL AND MORPHOLOGICAL FEATURES OF GASTRIC AND DUODENAL INVOLVEMENT IN THE EARLY STAGE OF OPISTHORCHIASIS. *(Rus.)* Karzin, V. V.; Tumol'skaia, N. I.; Ozeretskovskaia, N. N. (E. I. Martsinovskii Inst. Med. Parasitol. Trop. Med., Moscow, USSR). *Med. Parazitol. (Mosk.)* 41(4):387-391, 1972.

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8207 ENDEMIC HEPATIC ANEBIASIS: EIGHT CASES. *(Fr.)* Capron, A.; Wattre, P.; Capron, M.; Lefebvre, M. N. (Univ. Hosp. Ctr., Lille, France). *Lille Med.* 17(7):956-959, 1972.

See also, 6719, 6740, 6797, 6809, 6812, 6839, 7292.

GENERAL

Regional Enteritis

8208 PROGNOSIS AFTER COLONIC RESECTION FOR CROHN'S DISEASE OF THE COLON. *(E.)* Nugent, F. W.; Veidenheimer, M. C.; Meissner, W. A.; Haggitt, R. C. (Lahey Clin. Fnd., Boston, Mass.). *Gastroenterology* 65(3):398-402, 1973.

Case records and histologic sections of 115 consecutive patients undergoing colectomy for inflammatory disease of the colon from 1957 to 1959 were reviewed. Clinical and histologic criteria revealed ulcerative colitis (59 patients), Crohn's disease of the colon (44), and indeterminate colitis (12). Of the 44 with Crohn's disease, 33 had ileostomy and proctocolectomy as the initial or subsequent operative procedure. Recurrent Crohn's disease in the ileum developed in 1 patient (3%) during the prolonged follow-up period. Care must be taken to differentiate recurrent Crohn's disease from ileal stomatitis. The prognosis of Crohn's disease of the colon after ileostomy and proctocolectomy is very good, and if all disease is resected at operation, recurrence is unusual. This is not to suggest that ileostomy and proctocolectomy are necessarily the procedures of choice. If the patient's rectum is normal and the perineum is not involved, an anastomotic procedure may be used, even though recurrence is likely.

8209 USE OF PARENTERAL NUTRITION IN TREATMENT OF ADVANCED REGIONAL ENTERITIS. *(E.)* Anderson, D. L.; Boyce, Jr., H. W. (Walter Reed Army Med. Ctr., Washington, D.C.). *Am. J. Dig. Dis.* 18(8):633-640, 1973.

Advanced regional enteritis characterized in 8 patients (7 males and 1 female, aged 16-62 yr) by multiple areas of involvement, previous surgery (5 of 8), and failure on medical therapy (6 of 8) was treated by total parenteral nutrition for 30 days. The infusion solution was obtained by mixing hyperalimenation kits containing dextrose and casein hydrolsate. After mixing, each liter of solution provided 1000 carbohydrate calories, 50 g protein, and a total of 93 mEq of electrolytes including Na^+, K^+, Cl^-, Ca^{++}, and PO_4. From 3000-3500 non-protein calories and 150-175 g protein were infused daily in all patients. Nothing was administered by mouth except 2 eggs given every 10 days to stimulate emptying of the gall bladder. In 8 of 9 courses administered, improvement marked by weight gain, diminished pain, decreased diarrhea, and increased serum albumin from 2.9-4.4 g/100 ml was found. However, clinical remission was transient in 7 of 8 successful courses, ranging from 2 weeks to 14 months, indicating that parenteral nutrition is not a definitive form of therapy. The results suggest that parenteral nutrition may be useful in patients with regional enteritis to restore nutrition, induce remission, and prepare a debilitated patient for surgery. Additional experience is required to determine the efficacy of parenteral nutrition for therapy of fistulae caused by regional enteritis. Acute acalculous cholecystitis developed in 1 patient, possibly due to stagnation of bile flow and gallbladder failure during parenteral nutrition. This patient subsequently developed staphylococcal sepsis during his second course of parenteral nutrition. Mildly abnormal liver functions occurred in 5 patients, and were characterized by modest elevations of SGOT (75-150 U, and alkaline phosphatase (18-24 King-Armstrong U). Hyperosmolar coma, venous thrombosis, or hypophosphatemia did not occur in this study.

8210 THE SKIN IN PATIENTS WITH CROHN'S DISEASE AND ULCERATIVE COLITIS. *(E.)*

Verbov, J. L. (St. Bartholomew's Hosp., London, England). *Trans. St. John's Hosp. Dermatol. Soc.* 59(1):30-36, 1973.

A study was made of skin lesions and/or oral ulceration in 101 patients with Crohn's disease (45 males aged 13-80 yr and 56 females aged 15-66 yr) and 40 with ulcerative colitis (19 males aged 16-68 yr and 21 females aged 22-71 yr). Of the patients with Crohn's disease, 15 (4 males and 11 females) gave no history of skin problems. Skin conditions in the remaining patients with Crohn's disease and ulcerative colitis resp., included acne (12) (6); rosacea or telangiectasia alone (8) (3); infections (10) (3); psoriasis (5) (3); atopy (8) (1); non-atopic dermatitis, dry skin, ichthyosis, and prurigo (15) (8); anal and perianal conditions (28) (0); vascular conditions (19) (5); oral lesions (19) (4); finger clubbing (2) (0); hyperpigmentation (4) (0); vitiglio (0) (3), seborrheic warts (0) (1), and genital or perianal conditions (0) (3). Thus 85.1% of patients with Crohn's disease and 75.0% of the patients with ulcerative colitis reported difficulties along these lines. It is clear that many of these conditions resulted from therapy rather than from the diseases themselves.

8211 URINARY TRACT COMPLICATIONS IN REGIONAL ENTERITIS. *(E.)*

Steigmann, F. (Hektoen Inst. Med. Res., Chicago, Ill.). *Am. J. Gastroenterol.* 59(5):389-396, 1973.

An analysis was made of clinical findings in 7 of 64 patients with regional enteritis who developed urinary complications. Of these 7 patients, 6 (5 men and 1 woman) were less than 30 yr old (average 22 yr) and had histories of regional enteritis dating back 2-12 yr. The remaining patient was a 64-yr-old man who had been treated for more than 20 yr. Only 2 patients had involvement of the colon. All patients had intermittent abdominal pain, distention, diarrhea, and low-grade fever. No significant urinary symptoms became manifest until the final attack which was accompanied by marked urgency, dysuria, and suprapubic pain. In contrast to another report in the literature, no pain was observed in the right hip with radiation to the thigh. One patient had hematuria and 1 had fever and pain the lower abdomen which responded to chloramphenicol (500 mg every 6 hr) within 12-24 hr. Only 1 patient had colic-like symptoms; he was later found to have uric acid calculi. Laboratory tests did not contribute significantly to diagnosis of urinary complications, and x-ray studies showed only changes characteristic of regional enteritis. The lack of abnormal urinary findings suggests that ureteral obstruction is extrinsic, rather than intrinsic with infection It is recommended that the affected part of the intestine be resected since a diseased intestinal loop may still continue as the source of inflammatory compression of the ureter. Patients with all forms of regional enteritis should have frequent excretory urography to determine the status of the right ureter and right kidney.

8212 THE EFFECT OF LONG-TERM STEROID THERAPY ON THE HISTOPATHOLOGY OF REGIONAL ENTERITIS. *(E.)*

Max, M. H.; Wolff, M.; Broell, J. R.; Gump, F. E. (Coll. Phys. Surg., Columbia Univ., New York, N.Y.). *J. Surg. Res.* 14(2):124-132, 1973.

The incidence of 11 histological features was analyzed by step-wise discriminant analysis in 64 patients (38 men and 26 women, aged 17-48 yr) with regional enteritis who had not received steroids and in 16 patients (7 men and 9 women, aged 17-53 yr) with regional enteritis who had been treated with prednisone (mean dose of 10-35 mg/day for 2-36 months). All patients in both groups had been treated by ileocolostomy, and all patients in the steroid-treated group had disease limited to the small intestine. The 11 features selected were pyloric metaplasia, granulomas of the intestinal wall, lymph node granulomas, neuromatous lesions, vascular lesions, microscopic abscesses, microscopic fistulas, lymphatic dilatation, lymphoid nodules, hypertrophy of the muscularis mucosae, and cysts. Steroids did not reduce the incidence of chronic proliferative changes such as sarcoid-like granulomas. Histological changes were similar in steroid-treated and -untreated patients, but the incidence of microscopic fistulas and dilated lymphatics was significantly higher in steroid-treated patients. These findings suggest that steroids do not have a beneficial effect on regional enteritis although they do produce symptomatic clinical improvement.

8213 A FURTHER CASE OF CHRONIC ULCERATIVE ENTERITIS. *(E.)*

Armstrong, B. K.; Ammon, R. K.; Finlay-Jones, L. R.; Joske, R. A.; Vivian, A. B. (Dept. Med., Univ. Western Australia, Perth). *Gut* 14(8):649-652, 1973.

A 58-yr-old female presented with a 20 yr history of epigastric pain and flatulence accompanied by progressive lassitude, diarrhea, nausea, vomiting and lower abdominal pain. A narrow irregular segment of sigmoid colon was seen on barium enema examination. Laparotomy showed several sigmoid diverticula. Atrophic jejunitis and intestinal malabsorption persisted after surgery, and a barium meal showed dilated loops of small bowel and coarse jejunal mucosal folds. Jejunal biopsy revealed subtotal villous atrophy. Therapy consisting of a gluten-free diet, plus potassium, calcium, and folic acid supplements was unsuccessful. Oral tetracycline, pancreatic extract, and prednisone were also unsuccessful. A second and third laparotomy were performed, each followed by temporary improvement. At the final laparotmy a diagnosis of malignant obstruction was made. A resection of 62 cm of the small bowel was made, and examination of the specimen showed 2 large deep circumferential ulcers plus 13 other shallow ulcers distributed in irregular fashion along the mucosa. A mixture of gram-positive cocci and bacilli were found on the surface, but no acid-fast organisms or fungi were present. Arteritis adjacent to ulceration is thought to be a secondary effect. The presence of bacteria in the ulcerated areas of mucosa in this case does not explain the chronicity of the disease nor its clinical and histological differences from known bacterial ulcerative diseases of the small intestine. There was no evidence that potassium chloride supplements given this patient were responsible for the ulceration. Steroid and antibiotic therapy are of questionable benefit in such cases. Surgery is necessary both for diagnosis and treatment of obstructing lesions.

8214 TOXIC MEGACOLON IN GRANULOMATOUS COLITIS. *(E.)* Anselm, K.; Rosenblum, S. A.; De Marco, V. (Henry Ford Hosp., Detroit, Mich.). *Henry Ford Hosp. Med. J.* 21(2):69-74, 1973.

In a 10-yr period toxic megacolon developed in 14 patients with ulcerative colitis and in 12 with granulomatous colitis. Of the patients with granulomatous colitis, all but 1 had the disease for more than 3 months prior to an acute exacerbation with distension of the colon; in 7 cases the colitis involved the entire bowel. Treatment with antibiotics and systemic corticosteroids was unsuccessful in all but 2 patients, and surgery had to be performed because of persistent distension in 10 cases. Free or walled-off perforations had developed in 5 of these patients. Two patients died postoperatively of peritonitis and septicemia which were casued by multiple perforations of the small intestine and an anastomotic leak, resp. In contrast to radiological findings in ulcerative colitis, those in granulomatous colitis showed fewer segments of distension, no distension of the sigmoid, and a higher incidence of large pseudopolyps. These findings suggest that toxic megacolon occurs more commonly in granulomatous colitis than has been reported and is a more serious complication than toxic megacolon in ulcerative colitis.

8215 EPIDEMIOLOGY OF REGIONAL ENTEROCOLITIS (CROHN'S DISEASE) AND ULCERATIVE COLITIS. *(E.)* Myren, J. (Ulleval Hosp., Univ. Oslo, Norway). *J. Abdominal Surg.* 15(7):127-130, 1973.

A retrospective study was made of regional enterocolitis (Crohn's disease) and ulcerative colitis as they occurred in Norway during 1956-1963. The incidence of Crohn's disease was 2.6/million/yr and was similar in both sexes. There were 2 peaks in age, 20-30 yr and 50-60 yr, during which most of the cases were found. In ulcerative colitis the highest incidence occurred in the 20-40 yr age groups, about equally for both sexes. The ratio of ulcerative colitis to regional enteritis was about 8 to 1. In the following 5-yr period, the incidence of Crohn's disease was 3 times higher. Ulcerative colitis had increased from 23 to 33 cases/million/yr. A similar study conducted in Great Britain showed the incidence of ulcerative colitis was 2 times higher than in Norway, and that of Crohn's disease 3 times higher. As noted in the Norway series, Crohn's disease was rarely seen in children. There seemed to be a higher incidence in Jews in Great Britain. In the United States the annual incidence of ulcerative colitis was 46 cases/million, while that of Crohn's disease was 18 cases/million. A bimodal occurrence was found for females in Crohn's disease, which showed the highest incidence in Jews. In Sweden the incidence of Crohn's disease was 25/million. In Denmark the incidence was 73 cases/million. For all countries, there was a family accumulation in about 5% or less of the cases, indicating that heredity may not be significant in etiology of the two diseases.

8216 ABSORPTIVE DEFECTS IN YOUNG PEOPLE WITH REGIONAL ENTERITIS. *(E.)* Beeken, W. L. (Dept. Med., Univ. Vermont, Burlington). *Pediatrics* 51(1):69-74, 1973.

Crohn's disease in 11 patients (8 males and 3 females, aged 8-21 yr) was evaluated to document the incidence and severity of correctable nutritional deficiencies in young people with this disorder. Studies included common hematological and electrolyte determinations, complete gastrointestinal barium studies, assessment of d-xylose, vitamin B_{12} and fat absorption, and quantification of intestinal protein loss. A variety of abnormalities was found including subnormal weight, diffuse disease radiologically, anemia, low serum iron, and excessive protein loss, all of which occurred in 8 patients. Vitamin B12 malabsorption and hypoproteinemia occurred in 6 and steatorrhea and hypocalcemia were detected less often. It is suggested that children with Crohn's disease be carefully monitored for absorptive defects which are amenable to corrective or palliative treatment.

8217 THE IMMUNOGLOBULIN CONCENTRATIONS IN SERUM AND BOWEL SECRETION IN PATIENTS WITH CROHN'S DISEASE. *(E.)* Bergman, L.; Johansson, S. G. O.; Krause, U. (Univ. Hosp., Uppsala, Sweden). *Scand. J. Gastroenterol.* 8(5):401-406, 1973.

Concentrations of IgG, IgA, IgM, and IgE were measured in 55 patients (36 males and 19 females, aged 15-62 yr) with Crohn's disease in different stages of activity; 15 patients were being treated with prednisolone (5-15 mg/day). IgG, IgA, and IgM concentrations were the same as those of 89 normal adults. The activity of the disease and corticosteroid therapy had no effect on the concentrations of these immunoglobulins. No IgA at all was found in 3 patients with active Crohn's disease; the expected percentage in the normal population is about 0.2%. In Crohn's disease IgE concentrations were somewhat lower than those in 150 normal adults, but the difference was not statistically significant. No difference was found between the immunoglobulin concentration in venous and arterial blood from a segment of the bowel involved with Crohn's disease or ulcerative colitis. The albumin concentration and IgG/albumin ratio were increased in secretion from the diseased intestine; ratios of IgA and IgE to albumin were normal.

8218 ADENOCARCINOMA AND CROHN'S DISEASE. A REPORT OF 2 CASES AND ANALYSIS OF THE LITERATURE. *(E.)* Darke, S. G.; Parks, A. G.; Grogono, J. L.; Pollock, D. J. (London Hosp., England). *Br. J. Surg.* 60(3):169-175, 1973.

A 60 yr old male patient was admitted with a 45 yr history of attacks of partial small bowel obstruction which had become more severe and were accompanied by watery diarrhea during the past 2 yr. Crohn's disease, found at operation, involved the terminal 38 cm of the ileum. Immediately proximal to the diseased bowel lay a large fecalith. A fissure extended through the muscle coat of the bowel, and directly above this point, a well-defined adenocarcinoma infiltrated the full thickness of the ileum. An *in situ* carcinoma was present in the adjacent bowel and it extended to the opening of the fissure. A 67 yr old female presented with a 2 month history of diarrhea, rectal bleeding, and weight loss. Crohn's disease, extending from the mid-transverse colon to the rectum was seen on barium enema examination. Almost 1 yr later, sections from the nodules at 13 cm from the anus showed the rectum was invaded by a well-differentiated adenocarcinoma extending through the submucosa and slightly invading the inner muscle coat. The tumor surface had a villous pattern. Crypt abscesses were occasionally seen, but only near areas of ulceration. From these cases, and others already reported in medical literature, it is concluded that there is a small but significant risk of carcinoma developing both in large and small intestines in the course of Crohn's disease.

8219 MICROBIAL FLORA OF THE UPPER SMALL BOWEL IN CROHN'S DISEASE. *(E.)* Beeken, W. L.; Kanich, R. E. (Coll. Med., Univ. Vermont, Burlington). *Gastroenterology* 65(3):390-397, 1973.

Aerobic and anaerobic microflora were quantified in 36 patients with Crohn's disease and correlated with the location of radiological abnormality, intestinal protein loss, and absorption of *d*-xylose, fat, and vitamin B_{12}. Jejunal colony counts of 10^4/ml or greater were detected in 11 patients, designated as a high-colony group. In this group 8 patients had 22 absorptive defects, 7 of which were attributed to bacterial overgrowth alone and 15 were associated with a combination of high colony counts and disease or resection of the absorptive site. In the high colony group 3 patients had normal xylose, fat, and B_{12} absorption. Organisms isolated from this group were *Escherichia coli*, Clostridia, bacteroides, *Propionibacterium acnes*, streptococci, enterobacter, Veillonella, and *Candida albicans*. In the low-colony group, 7 patients had no absorptive abnormality, and the remainder had 20 defects attributed to the location of disease or resection, and 7 unexplained defects. Excess protein loss and high urinary indican values were present in 27 patients and neither correlated with bacterial colony counts. Jejunal disease and enteroenteric fistula were more frequently associated with high colony counts and may have predisposed to jejunal contamination. Quantitative small bowel culture is therefore indicated in patients with Crohn's disease who have multiple absorptive defects, especially if accompanied by jejunal disease or enteroenteric fistulae.

8220 THE DIAGNOSIS OF IRON DEFICIENCY IN PATIENTS WITH CROHN'S DISEASE. *(E.)* Child, J. A.; Brozovic, B.; Dyer, N. H.; Mollin, D. L.; Dawson, A. M. (St. Bartholomew's Hosp., London, England). *Gut* 14(8):642-648, 1973.

A selected group of 21 patients with Crohn's disease (9 males and 12 females, aged 15-46 yr) who had a routine peripheral blood picture suggestive of iron deficiency were studied. Only 9 (43%) of these patients had no stainable iron stores in the bone marrow fragments and could be considered definitely iron deficient. Of these 9, dietary inadequacies seemed responsible for the iron deficiency in 4 patients. A further 9 patients had reduced iron stores. Increased iron stores occurred in 2 patients. All direct measurements in the diagnosis of iron deficiency, except the total iron-binding capacity, appeared likely to result in overdiagnosis. Iron-deficient erythropoiesis, without true deficiency, may be due to the inflammatory disease process and this study indicates that the examination of bone marrow aspirate is necessary for the certain diagnosis of iron deficiency in Crohn's disease.

8221 CROHN'S DISEASE: A CLINICAL STUDY OF 75 PATIENTS. *(E.)* Arvanitakis, C.; Manier, C. W. (St. Joseph's Hosp., Marshfield, Wis.). *Am. J. Gastroenterol.* 59(6):532-540, 1973.

The case records of 75 patients (34 males and 41 females) with Crohn's disease, seen in a 14 yr period and followed up for periods of 1-10 yr, were reviewed to determine the outcome of their medical and surgical treatment. Mean age of the patients at onset of disease was 24.2 yr; the most common presenting symptoms were abdominal pain (56 patients), diarrhea (41), and weight loss (41). Of the 75 patients, 55% had ileitis only, 33.3% ileitis and granulomatous colitis, and 10.7% colitis only. Anemia was present in 50%, leucocytosis in 20%, and hypoalbuminemia in 20%. Liver involvement was mild and clinically un-important. Corticosteroids alone or combined with salicylazosulfapyridine induced a remission in 75% of the patients, which ranged from 6 months to 5 yr. Following radical resection of the affected bowel, marked clinical improvement was initially noted in the 53 patients requiring surgery for complications or failure of medical treatment. However, the cumulative relapse rate was 56%, with 23% of this number requiring more than 1 operation.

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8230 PARESTHESIAS AND HYPOPHOSPHATEMIA OCCURRING WITH PARENTERAL ALIMENTATION. *(E.)* Sand, D. W.; Pastore, R. A. (Fitzsimons Army Med. Ctr., Denver, Col.). *Am. J. Dig. Dis.* 18(8):709-713, 1973.

8231 PROLIFERATIVE ILEITIS OF HAMSTERS: ELECTRON MICROSCOPY OF BACTERIA IN CELLS. *(E.)* Wagner, J. E.; Owens, D. R.; Troutt, H. F. (Sch. Vet. Med., Univ. Missouri, Columbia). *Am. J. Vet. Res.* 34(2):249-252, 1973.

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8234 OBSTRUCTIVE UROPATHY IN GRANULOMATOUS BOWEL DISEASE. *(E.)* Mooney, R. A. H.; Sant, G. R. (Trinity Coll., Dept. Surg., Dublin, Ireland). *Br. J. Surg.* 60(7):525-527, 1973.

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PREFACE

GASTROENTEROLOGY ABSTRACTS and CITATIONS is a publication of the National Institute of Arthritis, Metabolism and Digestive Diseases. This specialized information medium has been initiated to fill an existing great need in the field of gastroenterology and to assist the Institute in meeting its obligations to foster and support laboratory and clinical research into the nature, causes, and therapy of diseases of the gastrointestinal tract. Publication GASTROENTEROLOGY ABSTRACTS and CITATIONS makes available citations of all current papers relevant to this field from medical journals published throughout the world. Approximately one-third of the citations dealing with the major aspects of gastroenterology have accompanying abstracts.

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